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## Maternal trauma due to motor vehicle crashes and pregnancy outcomes: A systematic review and metaanalysis

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Maternal trauma due to motor vehicle crashes and pregnancy outcomes: A systematic review and meta-analysis

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#### Abstract

#### **Objectives**

To systematically review and quantify the effect of motor vehicle crashes (MVC) in pregnancy on maternal and offspring outcomes.

#### Design

Systematic review and meta-analysis of observational data searched from inception until July 1, 2018.

#### **Participants**

Studies were selected if they focused on the effects of exposure MVC during pregnancy vs. nonexposure, with follow up to verify outcomes in various settings, including secondary care, collision and emergency, and inpatient care.

#### **Data synthesis**

For incidence data, we calculated a pooled estimate per 1000 women. For comparison of outcomes between women involved and those not involved in MVC, we calculated odds ratios (OR) with 95% confidence intervals (CI). Where possible, we statistically pooled the data using the random-effects model. The quality of studies used in the comparative analysis was assessed using the Newcastle-Ottawa Scale.

#### Results

We included 19 studies (3,222,066 women) of which the majority was carried out in high-income countries (18/19). In population-level studies of women involved in MVC, maternal death occurred in 3.6 per 1000 (95% CI 0.25 to 10.42; 3 studies, 12,000 women; Tau= 1.77), and perinatal death in 6.6 per 1000 (95% CI 3.81 to 10.12; 8 studies, 47,992 women;  $I^2=92.6\%$ ). The pooled incidence of complications per 1,000 women involved in MVC was labour induction (276.43), preterm delivery (191.90) and caesarean section (166.65). Compared to women not involved in MVC, those involved had increased odds of placental abruption (OR 1.43, 95% CI 1.27 to 1.63; 3 studies, 1,500,825 women) and maternal death (OR 202.27; 95% CI 110.60 to 369.95; 1 study, 1,094,559 women). Pregnant women involved in MVC using seatbelts have a lower risk of fetal death (OR 0.66 95%CI 0.36 to 1.19).

**Conclusion:** Pregnant women involved in MVC were at a higher risk of maternal and fetal death, and complications than those not involved.

## PROSPERO registration: CRD42018100788

Key terms: Pregnancy; motor vehicle crashes; pregnancy complications

## Word count: 300

## Strengths and limitations of this study

- This is the first systematic review examining the link between involvement in MVC, mortality and adverse outcomes that includes evaluation of study quality assessment.
- This is the second systematic review looking at outcomes following MVC in pregnancy.
- We conducted our review using a prospectively registered protocol and reported it in accordance with the international standards.
- Outcomes variables correspond to any trimester, not to specific trimesters.
- Outcomes according to seatbelt use are scarce, since only two studies use population-level data.

## **Funding statement**

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## Competing interest's statement

There is non-financial associations that may be relevant to the submitted manuscript.

#### Introduction

Up to half of all women in developed countries drive motor vehicles (1) and the consequences of road traffic-related injuries involving pregnant women can be severe (2). Indeed, motor vehicle crashes (MVC) are the most common cause of non-obstetric trauma associated with fetal deaths (2.3 per 100,000 live births) (3) . The risk of adverse outcomes resulting from an MVC increases in the second trimester of pregnancy if the pregnant women were the driver (4); however, this does not appear to be the case for pregnant passengers or pedestrians (5). A maternal mortality rate of 3.5 women per 100,000 is reported following MVCs in pregnant women (6). Mechanisms of injury recorded within the pregnant population of the UK national trauma registry, the Trauma Audit and Research Network (TARN), saw an increased rate of vehicular collision in pregnant women when compared to the non-pregnant cohort (7). In 2001-2008, 2.9% of pregnant women in North Carolina were drivers in one or more crashes (8). In the USA, data from the National Automotive Sampling System (NASS/CDS) reflects that when vehicles with pregnant women are involved in an collision, 50% of those women will sustain an injury(9). There are few safety guidelines on travelling by car during pregnancy (10-12). The focus of these tends to be on questions around the use of seatbelts and the activation of airbags in the car (12).

There is a reported association between MVC and maternal mortality (13). Moreover, further associations such as the trigger for immediate delivery or being more likely to die are reported with severe blunt injury (Injury Severity Score (ISS) of 9 or above, or systolic blood pressure (SBP) <90mmHg on arrival) (14). Involvement in MVC is also associated with perinatal mortality (15), injuries to the abdominal region (16), placental abruption secondary to increased intra-abdominal pressure (17), preterm birth, and caesarean section (6). However, more data is required in relation to areas such as fetal outcomes and higher risk pregnancies, particularly regarding sociodemographic characteristics of the mother, specific trimester of pregnancy when exposed to trauma, socioeconomic country conditions, severity and type of trauma, and collision characteristics such as speed. A systematic review on trauma in pregnancy (including five studies reporting complications of involvement in MVC, and fourteen other studies on others form of trauma) showed that MVC and domestic violence were the most common causes of traumatic injury during pregnancy (4). No quality

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assessment of the included studies was reported in this review. Previous non-systematic reviews have published strategies used to monitor women and fetuses after a crash (18-21). However, to our knowledge there is no systematic review or meta-analysis focused on the maternal and fetal outcomes after MVC in pregnancy.

As the clinical impact on the mother and fetus after MVC has not been well documented, we conducted a systematic review of the effect on maternal and fetal outcomes of MVC in pregnant women, compared to those not involved in a collision.

#### Methods

We conducted a systematic review and reported it according to recommended standards (22). The review was prospectively registered with PROSPERO (no. CRD42018100788).

#### Literature search

The following databases were used to identify relevant literature: Medline, Embase, Web of Science, Scopus, LILACS (Latin-American and Caribbean System on Health Sciences Information), Science Citation Index, SciELO (Scientific Electronic Library Online), TRANSPORT, IRRD (International Road Research Documentation), TRANSDOC (European Conference of Ministers of Transportation databases), Cochrane Database of Systematic Reviews (CDSR), and Cochrane Central Register of Controlled Trials (CENTRAL). We also sought to identify unpublished research or research reported in the grey literature by searching a range of relevant databases, including the Inside Conferences, Systems for Information on Grey Literature (SIGLE) and Dissertation Abstracts. Furthermore, the searches of the medical database were supplemented with the Internet search using a general search engine (e.g. Google, <u>www.google.co.uk/</u>) and safetylit.org. Language and date restrictions were not applied to electronic searches. Relevant studies were identified using a combination of, but not limited to, the medical subject headings (MeSH) and keywords for motor vehicle collision (OR road traffic collision OR crash OR collision) and pregnancy (OR pregnant women OR gravid women OR childbearing women OR maternal).

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Papers were selected if they studied the effects of exposure to trauma due to involvement in an MVC during pregnancy vs. non-exposure, with follow up to verify outcomes in various settings including secondary care, collision and emergency, and inpatient care. Observational studies (cohort studies, case-control design, non-intervention arms of randomised controlled trials) were included. Case series and case reports were excluded. Appendix 1 shows the search strategy for Medline (via Ovid) and Appendix 2 the excluded studies with reasons.

#### Data extraction and study quality assessment

Two reviewers (CAP & JR) independently extracted the relevant data from each full-text article and data were recorded using a standardized data extraction form. A data extraction form was piloted for each study design and amended as required. Discrepancies were resolved by consensus or by a discussion with a third senior author (ER). We extracted data on a) severe adverse maternal outcomes such as maternal death, miscarriage and preterm birth (<37/40 and <34/40); b) severe adverse fetal outcomes such as intrauterine death/stillbirth and neonatal death. Secondary outcomes were: a) individual components of maternal outcomes such as preterm labour, mode of delivery (vaginal delivery vs caesarean section), premature rupture of membranes (PROM), preterm premature rupture of membranes (PROM), placental abruption, chorioamnionitis/sepsis and maternal admission to an intensive care unit (ICU) or high dependency unit (HDU); b) individual components of fetal outcomes: respiratory distress syndrome, neonatal ICU admission, low birth weight (LBW) and small for gestational age (SGA).

We also extracted data on 1) adverse outcomes in pregnant women involved in MVC and their offspring in subgroups according to maternal characteristics (low, high and any risk), trimester of exposure, country (low and middle income, high income), type of trauma (penetrating, blunt, burns), severity of trauma (mild, moderate, severe), seatbelt use (yes, no), study quality (low, high); 2) risk factors for pregnancy complications following MVC such as maternal characteristics (age, parity, high risk pregnancy, gestational age), type of trauma, type of motor vehicle, type of collision, collision characteristic (stationary, high or moderate speed) and seat belt use.

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The quality assessment of studies was independently evaluated by two reviewers (JR and CAP) using the Newcastle-Ottawa Scale (23). This scale includes 8 items, 4 items about selection criteria of cases or cohorts in case-control or cohort designs, respectively; 2 items about comparability between groups (in both designs); and 3 items about exposure criteria in case-control designs and about outcomes in cohort designs. Any of those studies could be awarded a maximum of one star for each numbered item within the selection and exposure categories. A maximum of two stars could be given for comparability. For the incidence analysis, we considered six aspects (24): 1) representativeness of cohort; 2) design; 3) method of sampling; 4) adequacy of follow-up; 5) if the outcomes were adequately ascertained and 4) if measurement or misclassification bias were minimized. Studies without these features or with unclear reporting were classified to have a high risk of bias.

#### Data synthesis

We undertook random-effects meta-analysis to determine the odds ratios (OR) with 95% confidence intervals (CI) for maternal and offspring complications from MVC. We estimated heterogeneity between the included studies with Chi-Square test of Q (I2) excepting when not enough studies were in the meta-analysis (2-3), and we pooled the rates of maternal/fetal complications and reported with 95% CI. For each primary outcome, a meta-analysis was conducted for studies sufficiently homogeneous in terms of the characteristics of participants and exposure. The subgroup analysis was applied in: a) trimester of pregnancy during which the trauma occurred; b) maternal risk status (low, high, any risk); c) type of trauma; d) severity of trauma (using the ISS to categorize the severity of trauma sustained following MVC) (25); e) setting (low and middle income, high-income country); f) year of study publication: (before or after the introduction of mandatory seatbelt legislature in the country of study); and g) study quality according to the Newcastle and Ottawa Scale (23).

#### Results

#### Study selection

Out of 1,739 retrieved references, 19 studies met the eligibility criteria (Figure 1). Five of these reported data allowing us to compare pregnancy complications between pregnant women involved in MVC and those not involved in MVC (6, 26-29). The totality of the studies (n = 19) contributed to the analysis of the incidence of pregnancy complications among women involved in MVC (6, 17, 26-42).

#### Characteristics of included studies

The characteristics of included studies are in Table 1. Included studies were published between 1993 and 2016. Most of them were carried out in developed, high-income countries such as USA (14/18) (26, 28-31, 33-41), Sweden (1/19) (27), Kuwait (1/19) (17) and Israel (1/19) (42). The number of included pregnant women varies, ranging from 39 to 1,094,559. The data was sourced from hospital records/trauma registries (7/19) (17, 31, 32, 35, 38, 39, 42) or from population-level databases (12/19) (6, 26-30, 33, 34, 36, 37, 40, 41). The majority of studies collected information on outcomes of pregnant women involved in MVC during any trimester of pregnancy. 8 out of 19 studies reported information about the use of safety devices such as seatbelts and/or airbag (26, 29, 30, 33, 35, 37-39). Also in eight studies, the authors assessed the severity of MVC injuries with five of these using a validated tool (28, 31, 35, 38, 42) – most of them reporting ISS (28, 31, 35, 42) and one the Revised Trauma Scale (38).

#### Quality assessment

60% of studies had a low risk of bias with regards to the adequacy of representativeness and random sample selection (12/19). None of the studies was prospective. The categories of follow up of more than 80% of participants, outcome ascertainment and misclassification bias showed low risk (Figure 2). The five papers included for comparison of complication rates between pregnant women exposed to MVC and those who were not exposed (assessed using the Newcastle-Ottawa Scale) showed generally high quality, with four papers scoring 9/9 (6, 26, 28, 29). The remaining paper scored 8/9, losing one point for the comparability as it did not control for any secondary factors (27).

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The assessment of adverse outcome incidence among women involved in MVC (using population-level data) demonstrated incidence estimations of 276.43 per 1000 for induction of labour (95%CI 262.54 to 290.54), 191.90 per 1000 for preterm delivery (95%CI 45.98 to 405.74), and 166.65 per 1000 for caesarean section (95%CI 47.34 to 339.00). The estimated incidence rates for other complications included 42.33 per 1000 for PROM, 17.08 per 1000 requiring admission to hospital, 16.14 per 1000 for placental abruption and 15.19 per 1000 for neonatal respiratory distress. A pooled incidence of maternal death was 3.60 per 1000 women (95%CI 0.25 to 10.42, 3 studies, 12,000 women, Tau=1.77). The pooled incidence of perinatal death per 1000 women was 6.60, (95% CI 3.81 to 10.12; 8 studies, 47,992 women; I<sup>2</sup>=92.6%) (Table 2). The representation of the maternal and offspring outcomes according to trauma severity are in appendices (Appendices 3 and 4). Using data from single hospital centres, the random pooled estimation for the incidence of admission to hospital was 117.92 per 1000 women (95%CI 109.82 to 126.40) (17, 38); for maternal death was 135.05 per 1000 women (95%CI 131.37 to 138.80) and for fetal death was 5.73 per 1000 women (95% CI 3.05 to 9.77) (Appendices 5 and 6).

#### Pregnancy complications in women involved vs not involved in motor vehicle crashes

We observed a statistically significant link between involvement in MVC and maternal death (OR 202.3, 95%CI 110.60 to 370.00; single study) (27) (data not shown in table or graphic). Figure 3 shows pooled results from population-level data, demonstrating a positive association between MVC and placental abruption (OR 1.43 95% CI 1.27 to 1.63). Two studies contributed data used in sensitivity analyses stratifying by seatbelt use, where the pooled estimation (26, 29) of fetal death decreased with seatbelt devices (OR 0.66 95% CI 0.36 to 1.19) (Figure 4, supplementary). The review manager forest plot displays a positive but not statistically significant association between fetal death and MVC without seatbelt use (OR 5.78 95% CI 0.17 to 201.12, Tau<sup>2</sup> = 6.51) (Figure 5, supplementary).

#### Discussion

### Statement of principal findings

This review estimated that for women involved in MVC, maternal death occurrence was 3.6 per 1000 and perinatal death 6.6 per 1000 women. Compared to women not involved in MVC, those involved

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had an increased odds of placental abruption, perinatal death, antepartum haemorrhage and maternal death. Pregnant women involved in MVC who use seatbelts have a lower risk of fetal death. The pooled incidence of complications per 1,000 women involved in MVC was, from the higher incidence to the lower, induction of labour, preterm delivery, caesarean section, premature rupture of membrane, and placental abruption (population level-data).

#### Strengths and weaknesses of this study

This is the second systematic review, after the one of Mendez Figueroa et al., in 2013 (4), looking at outcomes following MVC in pregnancy. We conducted our review using a prospectively registered protocol (PROSPERO) and reported it in accordance with the international standards (43). This review, to our best knowledge, is the first one examining the link between involvement in MVC, mortality and adverse outcomes that involves evaluation of study quality assessment; 14 studies looking at outcome incidence related to MVC (17, 30-42) and 5 studies comparing outcomes in pregnant women involved in MVC and those who were not (6, 26-29). We used established tools to assess outcome reporting quality for the incidence rates (44) and comparability (45). We included data from population-level and single centre studies, but the analysis and reporting of the results were independent in order to get precision and validity in the estimations. However, a couple of graphics of the maternal and offspring's outcomes incidences have been included as Appendix 3 and 4. Between August 2018 and September 2019, there have been no new studies eligible to include in the systematic review.

For the incidence analysis, we evaluated the quality of the 19 studies of this systematic review. The highest risk was in the design. None of the studies had a prospective design. The representativeness of cohort and the random method of sampling were other limitations of the quality of studies, with 7 out of 19 studies having a high risk of bias in these areas (17, 31, 32, 35, 38, 39, 42). However, the quality assessment of the five papers included for comparison of complication rates between pregnant women involved and not involved in MVC using the Newcastle-Ottawa Scale showed generally high quality, with four papers scoring 9/9 (6, 26, 28, 29).

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The weaknesses of this systematic review are as follows. Firstly, outcomes were not reported by trimester, with 13 out of 19 papers focused on MVC at any trimester. Secondly, outcomes, according to seatbelt use, are scarce as only two studies using population-level data looked at safety features as a stratification factor (26, 29). Two studies with data sourced from hospital records/single-site trauma registries (38, 39) and three studies utilising population-level databases (26, 29, 30) reported some outcomes regarding seatbelt-use. Thirdly, we found a limited number of relevant studies comparing outcomes between women involved and not involved in MVC. The majority of the studies were carried out in the USA (26, 28, 29) with most recent one published in 2013 (29). Fourthly, we found heterogeneity in the included studies, seven of them have been carried out using hospital records/single-site trauma registry (17, 31, 32, 35, 38, 39, 42) and twelve using population database (6, 26-30, 33, 34, 36, 37, 40, 41). Finally, in only eight studies did authors assess severity of MVC injuries, with only five of these using a validated tool (28, 31, 35, 38, 42). This was a challenge when aiming to analyse results according to the severity of the crash.

## Meaning of the study

The principle outcomes reported in the comparability studies, all of them cohort studies from population database, were perinatal death (4/5) (6, 26, 27, 29), placental abruption and any preterm delivery (3/5) (6, 28, 29), being the most strong association with MVC maternal death, but this outcome comes from a single population database study (27). The principles outcomes according to the population level in descendant order of incidence estimate per 1000 were the induction of labour, preterm delivery, caesarean section, premature rupture of membranes, and admission to hospital, placental abruption and maternal death. The pooled result using meta-analysis of proportion (random-effects model) was placental abruption (outcome reported in three studies) (6, 28, 29). In this systematic review, stratifying by seatbelt use, we appreciated a higher association of fetal death with a non-seatbelt use when pregnant women were involved in an MVC. Previous studies have shown that pregnant women wearing a seatbelt during their MVC are not at a significantly higher risk of adverse fetal outcomes than women with no MVC involvement (46), and airbags contribute to the protection of both pregnant drivers and their fetuses (47).

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The results from this systematic review and meta-analysis allow us to adopt primary prevention measures, recommendations and educational interventions related to the prevention of motor vehicle crashes in pregnancy, which should be incorporated into the primary care pregnancy guidelines.

#### Unanswered questions and future research

The effects of MVC in pregnant women is a specific field that requires further research and an improved methodological approach to determine the risks of adverse maternal and fetal outcomes.

Additional variables such as trauma severity, the position of the women in the car, use of seatbelt, deployment or non-deployment of an airbag, severity of the crash and gestational week of pregnancy should be recorded in relation to MVC exposure in order to allow more precision when analysing outcomes. A greater number of studies in a variety of global settings would also confer more consistency in the outcomes.

#### Conclusions

Pregnant women involved in MVC have a higher risk of maternal and fetal death and complications than those not involved. These risks are associated with not using seatbelt devices, and complications include induction of labour, preterm delivery and caesarean section. Road traffic authorities should be conscious and strict in targeting preventive measures in pregnant women at risk of MVC.

#### Word count: 3,032

#### Author's contribution

PM conducted literature searches and screened publications jointly with JR. CAP and JR extracted the data. CAP and ER drafted the manuscript and conducted the statistical analyses. KSK and ST designed the study review. CAP is the guarantor. Authors VMR, KB, ABC, ST and KSK gave critical revision of the manuscript. All authors had full access to the data and take responsibility for the data analyses. The corresponding author attests that all listed authors meet authorship criteria.

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## Data sharing Statement

No additional data available

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## Table 1. Characteristics of included studies

Study ID Author, year, Country	Design	Sample size	Time period	Inclusion criteria	Data source	Trimest er	Seatbelt use (with data)	Assessment of trauma severity (with data)	Method of assessing trauma severity	Maternal outcomes	Offspring outcomes
Population-leve	el data										
<b>Azar, 2005</b> USA	population-based matched retrospective cohort <i>(incidence only)</i>	5936	2003- 2011	Admitted to hospital following MVC while pregnant	Population-based cohort	any	no	no	N/A	Maternal death	
<b>Hyde, 2003</b> USA	retrospective cohort (incidence and comparison)	322704	1992- 1999	Pregnant drivers involved in MVC	Linked databases (police registry & birth/death certificates)	any	yes	yes	Study- specific definition <sup>1</sup>		Fetal death
Kvarnstrand, 2008 Sweden	retrospective cohort (incidence and comparison)	1094559	1991- 2001	Maternal inclusion on the accident register > 28 GW	Linked databases (police registry & birth/death certificates)	2 <sup>nd</sup>	no	yes	Study specific definition <sup>2</sup>	Maternal death	Fetal/neonatal death
<b>Kuo, 2007</b> USA	retrospective chart/database review (incidence only)	16982 injured 4479 (in MVC)	2002	Pregnant women hospitalized with injury (only MVC used)	Sample from population level cohort (National Inpatient Sample)	any	no	no	N/A	Delivery, hospitalization	
<b>Schiff, 2005</b> USA	retrospective cohort (incidence and comparison)	17899	1989- 2001	Hospitalized for MVC and with a singleton livebirth or fetal death	Linked databases (hospital discharge data & birth/death certificates)	any	no	yes	ISS	Preterm birth, PROM, C-section, placental abruption	Stillbirth LBW, SGA, Fetal distress, RDS, Meconium
Schiff, 2010 USA	retrospective cohort (incidence only)	3348	2002- 2005	Nonrollover MVC among pregnant front seat occupants	Linked databases (hospital discharge data & birth/death certificates)	any	yes (airbag) no (seatbelt)	no	N/A	Preterm birth, placental abruption, labour induction, C- section	Stillbirth, LBW SGA, RDS Fetal distress Meconium
Vivian- Taylor, 2012 Australia	retrospective cohort (incidence and comparison)	604380	2000-2007	Women who gave birth exposed and not exposed to MVC	Linked databases (hospital discharge data & birth/death certificates)	2 <sup>nd</sup>	no	yes	Study- specific definition <sup>3</sup>	Admission, placental abruption, APH,PPH, preterm birth, C- section	Perinatal death, neonatal transfer

<b>Vladutiu, 2013</b> USA	retrospective cohort (incidence and comparison)	878546	2001- 2008	Pregnant women 16-46 years, > 20GW, delivering a live/ stillbirth singleton infant	Linked databases (police registry & birth/death certificates)	2 <sup>nd</sup>	yes (seatbelt) yes (airbag)	no	N/A	Placental abruption, PROM, preterm birth	Stillbirth
<b>Weiss, 2002</b> USA	crash database pregnant vs. non- pregnant (NASS/CDS) (incidence only)	32810	1995- 1999	Pregnant and non- pregnant women 15–39 years	Sample from population-level database of traffic accidents	any	yes	no	N/A	Maternal death	
<b>Weiss, 2008</b> USA	retrospective cohort (incidence only)	1816	1999- 2002	Injury-related emergency department visits by pregnant women (only MVC used)	Linked databases (hospital discharge data & birth/death certificates)	any	no	no	N/A	Hospital admission	
<b>Whitehead, 2013</b> * USA	PRAMS survey database (incidence only)	235329	2000- 2005	Survey of women who recently delivered a live- born infant	Population-based cohort (PRAMS)	any	no	no	N/A	Preterm birth, UTI, PROM	
<b>Wolf, 1993</b> USA	population-based retrospective cohort (incidence only)	2582	1980- 1988	Pregnant women drivers involved in MVC >20GW	Linked databases (police registry & birth/death certificates)	2 <sup>nd</sup> & 3 <sup>rd</sup>	yes	no	N/A	Preterm birth, placental abruption, C-section	Stillbirth, LBW, RDS
Single hospita	l records/trauma reg	istry									
<b>Aboutanos, 2007</b> USA	retrospective chart/database review (incidence only)	148	2001- 2005	Pregnant women presenting to ED following MVC	Single hospital records from trauma centre	any	yes (only in miscarriage)	yes	ISS	Maternal death, miscarriage	Fetal death hydrops fetalis
Baerga- Varela, 2000 USA	retrospective chart/database review (incidence only)	39	1986- 1996	Admitted to hospital after MVC while pregnant	Single hospital records	any	no	yes	ISS	Maternal death, miscarriage	Stillbirth
<b>Brookfield, 2013</b> USA	retrospective chart/database review (incidence only)	256	1990- 2007	Pregnant women presenting to ED following MVC	Single hospital records from trauma centre	any	yes	yes	ISS and RTS	Maternal death, admission to hospital	

<b>Chibber,</b> 2015 Kuwait	retrospective chart/database review (incidence only)	728	2009- 2012	MVC, pregnant, treated at major tertiary hospitals	Single hospital records	2 <sup>nd</sup>	no	no	N/A	Maternal death, placental abruption, preterm birth, uterine rupture, C-Section, admission	Fetal death, fetal distress
<b>Luley, 2013</b> USA	retrospective chart/database review (incidence only)	126	1994- 2010	Pregnant women after an MVC >14/40 GA	Single hospital trauma database	2 <sup>nd</sup> & 3 <sup>rd</sup>	yes	no	N/A	Maternal death, placental abruption, C-section	Stillbirth
<b>Miller, 2016</b> Israel	retrospective cohort (incidence only)	3794	2006-2013	Women 18-40 years, in MVC and hospitalized (only pregnant cohort used)	National trauma registry	any	no	no	ISS	Maternal death, miscarriage, placental abruption, C-section	Stillbirth
<b>Orji, 2002</b> Nigeria	retrospective chart/database review (incidence only)	84	1980- 2000	Pregnant women in MVC managed in tertiary hospitals	Single hospital records**	any	no	no	N/A	Maternal death, placental abruption, uterine rupture, C-section	Perinatal death, fetal tachycardia

ISS: Injury Severity Score; RTS: Revised Trauma Score; ICU: Intensive Care Unit, N/A not applicable; GA: Gestational Age; LBW: Low birth weight; SGA: Small for gestational age; RDS: Respiratory distress syndrome. \*National survey; \*\*Two hospitals in same region included; <sup>1</sup>Possible/probable/incapacitated/fatal; <sup>2</sup>Fatal/major/minor/uninjured; <sup>3</sup> 'Severe' = admission to ICU and/or blood transfusion and/or injury to abdomen/pelvis/lower back.

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Table 2. Incidence of adverse outcomes per 1,000 women involved in motor vehicle crashes – data source: population databases

Outcome	Number of studies	Number of women	Incidence estimate per 1,000 women	95% CI
Maternal				
Maternal death	3	12000	3.60	(0.25 to 10.42)
Admission to hospital	2	3838	17.08	(13.20 to 21.46)
Placenta abruption	6	36737	16.14	(7.04 to 28.78)
Preterm delivery	5	265680	191.90	(45.98 to 405.74)
Premature Rupture of Membranes	3	260310	42.33	(5.87 to 109.24)
Labour induction	2	3930	276.43	(262.54 to 290.54)
Caesarean section	5	12338	166.65	(47.34 to 339.00)
Offspring	Ő'			
Fetal death	3	8210	5.97	(2.23 to 11.41)
Perinatal death	8	47992	6.60	(3.81 to 10.12)
Fetal distress	2	3930	60.09	(52.85 to 67.77)
Meconium at delivery	2	3930	52.61	(45.82 to 59.85)
Respiratory Distress Syndrom	3	6522	15.19	(5.83 to 28.68)

CI, Confidence Interval

## Figures

Figure 1. The study selection process in the systematic review of outcomes on pregnant women involved in motor vehicle crashes

Figure 2. The quality assessment of the included studies

Figure 3. Comparison of outcomes between women involved and not involved in motor vehicle crashes

Figure 4. (Supplementary). Comparison of pregnancy complication between women involved and not involved in motor vehicle crashes stratified by seatbelt use

Figure 5. (Supplementary). Comparison of maternal and fetal death between women involved and not involved in motor vehicle crashes stratified by seatbelt use

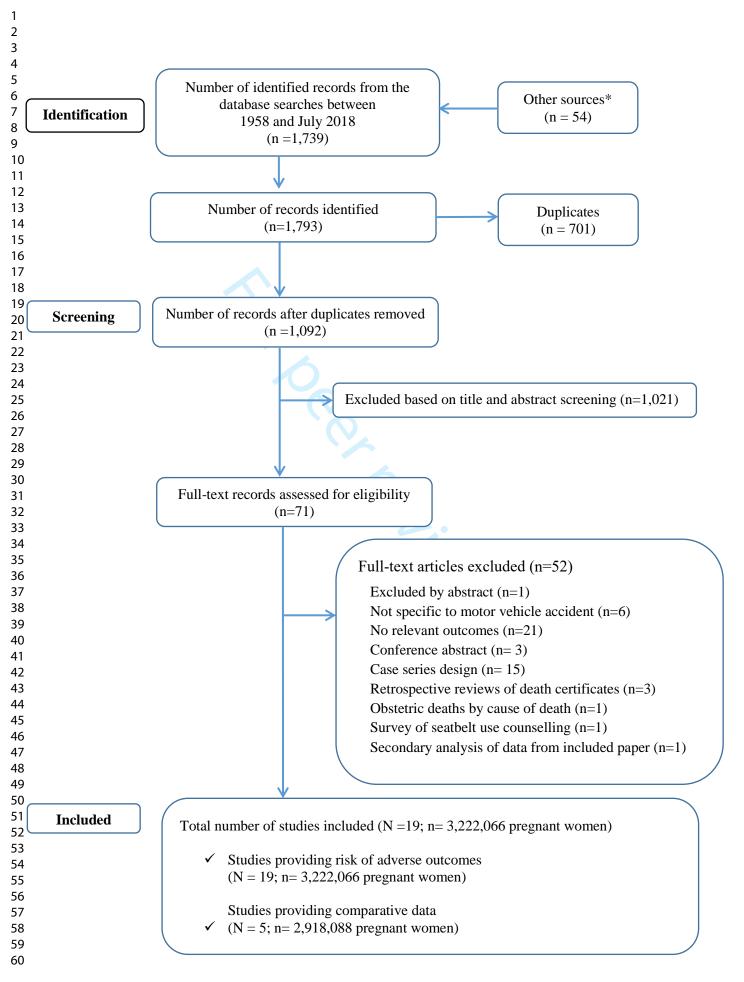
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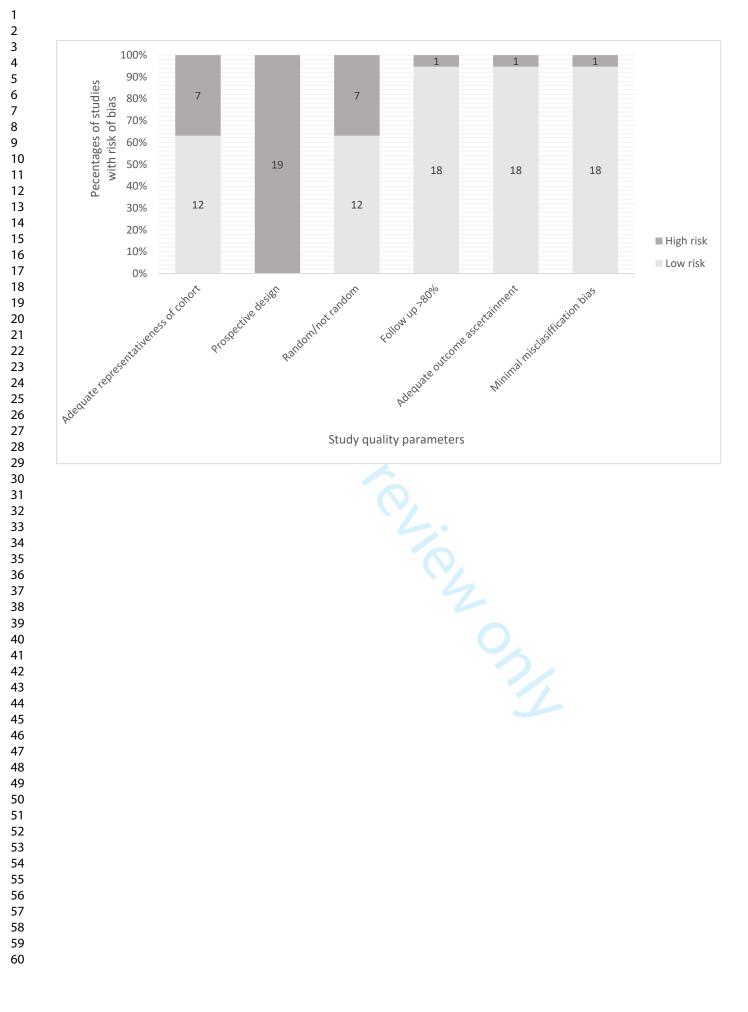
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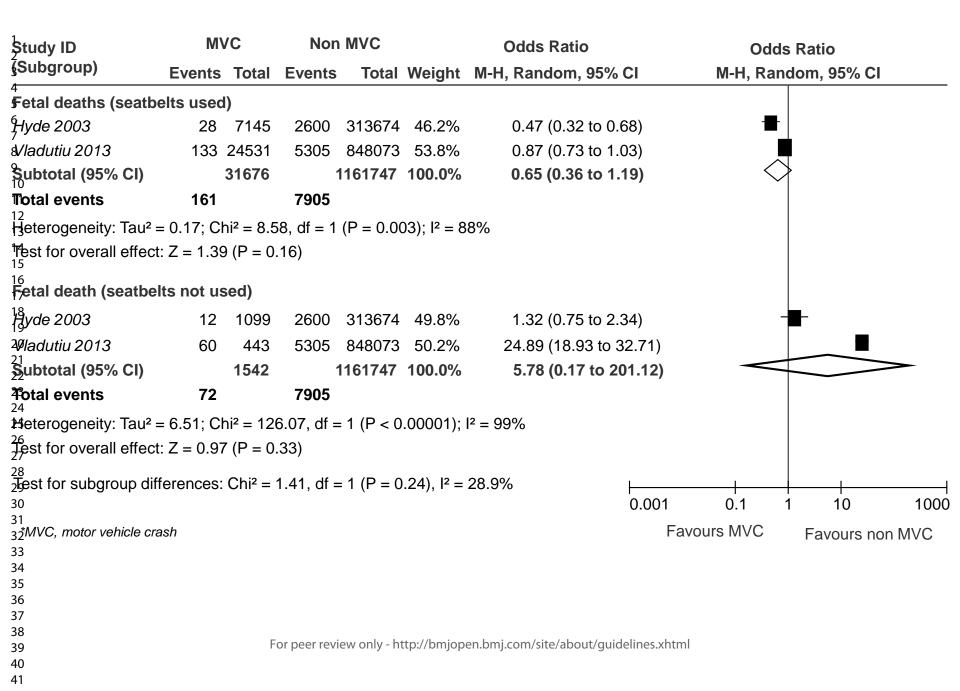
\*references of relevant non-systematic reviews and Google scholar



BMJ Open

Study ID		OR (95% CI)	Weigh
Perinatal death			
Hyde, 2003	<b>→</b>	0.61 (0.45 to 0.82)	29.18
Kvarnstrand, 2008	<b>_</b>	3.57 (2.44 to 5.23)	3.07
Schiff, 2005	$\rightarrow$	4.46 (2.01 to 9.91)	0.62
Vivian-Taylor, 2012	<b>←</b>	1.88 (1.34 to 2.65)	7.28
Vladutiu, 2013a	<b>-</b>	0.84 (0.71 to 1.01)	59.85
Subtotal (f² = 95.4%, p = 0.000)	$\diamond$	0.96 (0.84 to 1.09)	100.0
Cesarean delivery			
Schiff, 2005	-	1.41 (1.16 to 1.70)	17.21
Vivian-Taylor, 2012	+	0.98 (0.89 to 1.08)	82.79
Subtotal ( $P = 90.9\%$ , $p = 0.001$ )	$\diamond$	1.05 (0.97 to 1.15)	100.0
Placental abruption			
Schiff, 2005	<b>_</b>	6.45 (4.70 to 8.85)	4.25
Vivian-Taylor, 2012	<b>_</b>	3.30 (2.34 to 4.67)	5.70
Vladutiu, 2013a		1.08 (0.93 to 1.25)	90.05
Subtotal (f² = 98.4%, p = 0.000)	$\diamond$	1.43 (1.27 to 1.63)	100.0
Premature Rupture of Membranes			
Schiff, 2005	<b>◆</b>	1.11 (0.64 to 1.95)	2.09
Vladutiu, 2013a	◆	1.05 (0.97 to 1.14)	97.91
Subtotal (f² = 0.0%, p = 0.841)	Þ	1.05 (0.97 to 1.14)	100.0
Preterm delivery			
Schiff, 2005	_ <b>_</b>	6.52 (5.42 to 7.85)	1.00
Vivian-Taylor, 2012	-◆-	1.33 (1.13 to 1.55)	4.62
Vladutiu, 2013a	4	0.96 (0.92 to 1.00)	94.38
Subtotal (l² = 99.5%, p = 0.000)	p	1.03 (0.99 to 1.07)	100.0

Pa	ge 25 of 35 <b>Outcome</b>				BMJ Open	
1	Study ID	Overall incidence	Study size			OR (95% CI)
2 3	Fetal death					
4 5	Seatbelts not u	ised				
6	Hyde, 2003	1.176	2222			1.32 (0.74 to 2.33)
7 8	Vladutiu, 2013a	5.333	1006			<b>→</b> 21.65 (16.51 to 28.39)
9 10	Seatbelts used	l				
11	Hyde, 2003	.1832	14346		<b>—</b>	0.47 (0.33 to 0.69)
12 13	Vladutiu, 2013a	.1102	49328		◆	0.87 (0.73 to 1.03)
14 15		n				
16 17		ised				
18	Vladutiu, 2013a	.1152	49328	← ◆	-	0.02 (0.01 to 0.06)
19 20		I				
21 22		.1188	49328		+	1.09 (0.93 to 1.26)
23	Preterm delivery					
24 25		ised				
26	Vladutiu, 2013a	97.2	1006		-	0.85 (0.64 to 1.14)
27 28		I				
29	Vladutiu, 2013a	2.035	49328		•	0.94 (0.90 to 0.97)
30 31	Premature Rupture	Of Membran	es			
32 33		ised				
34	Vladutiu, 2013a	.388	49328			0.02 (0.01 to 0.04)
35 36		I				
37 38	viadulia, 2015a	.3993	49328	1 1	• • • • • • • • • •	1.03 (0.95 to 1.12)
39 40			For peer revi	•	njopen.bmj.com/site/aboµt/guidelines.xhtml-	
41				.00586	1	171



Item	Search term
1	pregnancy.af.
2	pregnan*.sh.
3	gravidity.sh.
4	gravid*.sh.
5	gestation*.sh.
6	pregnant women.sh.
7	pregnant wom#n.sh.
8	(child adj3 bearing).tw.
9	childbearing.af.
10	matern*.sh.
11	vehicle* crash*.af.
12	vehicle* accident*.af.
13	vehicle* collision*.af.
14	motor vehicle crash*.af.
15	motor vehicle accident*.af.
16	motor vehicle collision*.af.
17	motor vehicle injur*.af.
18	vehicle* injur*.af.
19	road traffic crash*.af.
20	road traffic accident*.af.
21	road traffic collision*.af.
22	road traffic injur*.af.
23	auto* crash*.af.
24	auto* accident*.af.
25	auto* collision*.af.
26	auto* injur*.af.
27	car crash*.af.
28	car accident*.af.
29	car collision*.af.
30	car injur*.af.
31	(car adj3 trauma).af.
32	(automobile adj3 trauma).af.
33	(automotive adj3 trauma).af.
34	(road traffic adj3 trauma).af.
35	(notor vehicle adj3 trauma).af.
36	1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10
37	11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or
	27 or 28 or 29 or 30 or 31 or 32 or 33 or 34 or 35
38	36 and 37

Appendix 1. Search strategy for MEDLINE (via Ovid) executed from database inception up to July 2018

Appendix 2 L	ist of exclude.	d studies v	with reasons
Appendix 2 E	list of cherude	a staares .	With reasons

ppendix 2 List of excl	uded studies with reasons	
Study ID	Reason	Reference
Al Mulhim, 2012	Pregnancy loss or not after trauma in Arabic pregnant women	EMHJ. Vol. 18 No. 5 2012
Battaloglu 2016	From a cohort of 15,140 female patients, 173 were pregnant women in the trauma registry. 55.5% of them from vehicle collision	SR Petrone, 2017 Injury, Int. J. Care Injured 47 (2016) 184-187
Barre 2006	Pregnant women with abdominal trauma during pregnancy (n=65). Half of them from a traffic accident.	<b>SR Petrone, 2017</b> La Revue Sage-Femme. Vol 5, Issue 6, 2006, 312-316
Cannada 2010	Pregnant women with orthopaedic injuries (n=65)	SR Petrone, 2017 Injury, Infection, and Critical Care.2010. Vol. 69 (3)
Chamberlain, 2011 🧹	Communication abstract. Retrospective cohort study. Identification of 272 pregnant trauma victims. 78.6% of them incurred in a MVC. No data to extract	American Journal of Obstetrics & Gynecology Supplement to January 2011
Cheng, 2012	Maternal complications during delivery according to uninjured, minor and severe injuries. 2,881 pregnant women (47,4%) involved in MVC	World J Surg (2012) 36:2767– 2775
Connolly, 1997	476 maternal records of trauma cases. 54.6% were MVC. No more data available	American Journal of Perinatology.1997.Vol. 14 (6)
Corsi 1999	Twenty-seven traumatised pregnant women were analysed retrospectively over a period of 9 years in Sao Paulo, Brazil	SR Petrone, 2017 Injury, Int. J. Care Injured 30 (1999) 239-243
Dannenberg, 1995	Homicide and other injuries as causes of maternal death between 1987 and 1991 in New York	Am J Obstet Gynecol Vol.172 (5)
Deshpande, 2017	Trauma impact on maternal mortality. Comparability between pregnant vs. non pregnant women	American Journal of Obstetrics & Gynecology 2017. 590.e2
El Kady 2004	Retrospective cohort study of women hospitalized for Trauma in California	SR Petrone, 2017 American Journal of Obstetrics and Gynecology (2004) 190, 1661-8
El Kady D, 2006	Fractures injuries on maternal/neonatal outcomes in United States	SR Méndez -Figueroa 2013 American Journal of Obstetrics and Gynecology (2006) 195, 711–6
Fischer 2011	Minor trauma and poor fetal outcomes in Tennessee, Memphis	SR Petrone, 2017 Injury, Infection, and Critical Care. 2011. Vol. 71 (1)
Gibbins, 2017	Communication. MVC and Stillbirth. Secondary analysis of 439 stillbirth	American Journal of Obstetrics & Gynecology Supplement to January 2017
Goodwin, 1990	Case-series of trauma pregnant women between 1987 and 1988 in Los Angeles	SR Méndez -Figueroa 2013 Am J Obstet Gynecol. 1990 Vol. 162 (3).

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Hardt, 2013	Prenatal risk screening to identify women at	Women's Health Issues 23-3
	increased risk for traumatic pregnancy-	(2013) e187–e193
	associated death	
Hardy, 1974	Maternal mortality ratios at large urban	Obstetric and Gynecology.
	charity hospitals from 1941 to 1971	1974. Vol.43 (1)
Harland 2014	Risks factors of maternal injuries in a	SR Petrone, 2017
	population-based sample of pregnant women	Journal of Women's Health.
	from Iowa	2014. Vol. 23 (12)
Hitosugi 2006	135 traffic accidents involving Japanese	SR Petrone, 2017
	pregnant women from insurance companies.	Forensic Science International
	The outcomes of neonates determined by	159 (2006) 51-54
	their condition 1 month after birth	
	(death/abortion/healthy)	
Ikossi, 2005	Risks factors of trauma in pregnant women	J Am Coll Surg. Vol. 2005. 200
	from San Francisco, California	(1)
Lynch, 2011	Pregnancy associated- death in Ohio: 2003-	American Journal of Obstetrics
	2007	& Gynecology Supplement to
		January 2011
Manoogian, 2015	Injuries characteristics between pregnant vs	Accident Analysis and
	non pregnant women occupants (not	Prevention 74 (2015).
	outcome)	69–76
Melamed 2012	Outcomes following blunt trauma in Pregnant	SR Petrone, 2017
	women from Israel	The Journal of Maternal-Fetal
		and Neonatal Medicine. 2012;
		25(9): 1612–1617
Mesdaghinia, 2012	Causes of trauma in 32 pregnant women with	Arch Trauma Res.
	trauma in a Hospital in Iran	2012;1(1):23-26
Nannini, 2008	Risks of injury in pregnant women in	Journal of Midwifery &
	Massachusets	Women's Health.2008. Vol.53
		(1)
Omoke, 2013	Trauma during pregnancy in a Nigerian	Int J Crit Illn Inj Sci. 2013; 3(4):
	setting	269–273.
Osei-Ampofo, 2016	A cross-sectional study with 134 pregnant	African Journal of Emergency
	women from Ghana visiting the emergency	Medicine (2016) 6, 87 –93
	care. Leading injury MVC (23%). Not	
	outcomes	
Pak, 1998	Delivery outcomes after a blunt abdominal	Am J Obstet Gynecol. 1998.
	trauma in 85 pregnant women 🥢	Vol. 179 (5)
Patteson, 2007	High risk factors involved in trauma during	The Journal of TRAUMA Injury,
	pregnancy. Not outcomes	Infection, and Critical Care.
		2007. Vol 62 (4)
Pearlman, 1990	Not possible to assess full text	SR Méndez -Figueroa 2013
Cab:ff 1007	Cost Doolt use Drotestive factor of maternal	W/144 1007 Vol 167 (1)
Schiff, 1997	Seat Bealt use. Protective factor of maternal	WJM, 1997. Vol. 167 (1)
<u> </u>	mortality after a MVC in Mexico	
Schuster, 2016	Communication abstract. Impact of blunt	American Journal of Obstetrics
	trauma on maternal and pregnancy outcome.	& Gynecology. Supplement to
	MVC the most common injury mechanism	January 2016
	(70%). Pennsylvania Trauma Systems	
	Foundation Database (1996-2013).	
Schuster, 2018	Pennsylvania Trauma Systems Foundation	Trauma, 2018. Vol. 20(1) 30–37
Schuster, 2018	Pennsylvania Trauma Systems Foundation Database. ISS>9 and SBP<90mmHg are	Trauma, 2018. Vol. 20(1) 30–37
Schuster, 2018	Pennsylvania Trauma Systems Foundation	Trauma, 2018. Vol. 20(1) 30–37

Sela, 2011	Treatment provided to pregnant motor vehicle accident (MVA) casualties in a mature trauma system in Israel	Annals of Surgery, 2011.Vol.254 (2)	
Shah, 1998	Trauma in general in pregnant women	J Trauma. 1998 Jul;45(1):83-0	
Shakerian 2015	Determining adherence to recommended imaging guidelines in pregnant women from Victoria, Australia	SR Petrone, 2017 J Trauma Acute Care Surg. 2015.Vol. 78 (1)	
Shiff 2002Retrospective cohort study to assess outcomes of pregnant women hospitalized for injury in Washington State from 1989 to 1997		<b>SR Petrone, 2017</b> J Trauma. 2002; 53: 939–945.	
Sirin, 2007	Report the prevalence of seatbelt counselling by prenatal care providers during pregnancy in USA	Matern Child Health J (2007) 11:505–510	
Tinker 2010 🥏	Risks factors involved in injuries in pregnant women from the National Birth Defects Prevention Study, USA	SR Petrone, 2017 Journal of Women's Health. 2010. Vol. 19 (2)	
Van der Knoop, 2015Effect of maternal trauma in fetal motility at term and at one year of age		Early Human Development 91 (2015) 511–517	
Van der Knoop, 2018Matched case-control study. Neuro outcome in 6-18 year old children a trauma in pregnancy			
Vladutiu, 2013b Same sample Vladutiu 2013a; exclud secondary analysis from already incl study		Accid Anal Prev. 2013; 55: 165 171	
Wahabi, 2007	45 MVC case series pregnant women collected over a 10- year period	Saudi Med J. 2007. Vol. 28 (9)	
Wall 2014	Pregnant trauma patiens from South Africa (mainly assaults)	<b>SR Petrone, 2017</b> Injury, Int. J. Care Injured 45 (2014) 1220–1223	
Weiner 2016	Minor trauma during pregnancy, not associated with adverse pregnancy outcomes, Israel	SR Petrone, 2017 European Journal Of Obstetrics & Gynecology and Reproductive Biology 203 (2016): 78–81	
Weiss, 1999 Retrospect review of death certificates		43rd Annual Proceedings Association for the Advancement of Automotive Medicine September 20-21, 1999. Barcelona (Sitges), Spain	
Weiss, 2001	Retrospect review of death certificates	JAMA, 2001. Vol. 286 (15)	
Weiss, 2002a	N/A		
Zangene, 2015	102 cases of trauma in pregnancy registered in Iran from 2007 to 2010. MVC the most frequent (45%)	Global Journal of Health Science. 2015. Vol 7 (2)	

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## maternal outcomes

1 2				
2 3 4	Study		ES (95% CI)	Trauma_severity
5	Placental abruption			
6	Wolf, 1993	1 Contraction of the second	8.10 (5.02, 12.36)	NK
7	Miller, 2016	1 Contraction of the second seco	1.05 (0.29, 2.70)	NK
8	Schiff, 2005		130.95 (67.22, 222.24)	severe
9	Schiff, 2005		126.21 (91.31, 168.48)	mild
10			. , ,	
11	Schiff, 2005		127.23 (95.92, 164.27)	mild-severe
12	Schiff, 2010	The second s	12.25 (8.80, 16.58)	mild
13	Vivian-Taylor, 2012	The second s	16.32 (11.26, 22.84)	mild-severe
14	Vladutiu, 2013a	The second s	7.17 (6.15, 8.31)	NK
15	Subtotal (I^2 = 96.7%, p = 0.00 🔇 🛇	1	15.41 (9.52, 21.30)	
16		1		
17	Admission to hospital			
18	Vivian-Taylor, 2012		8.90 (5.28, 14.03)	mild-severe
19	Weiss, 2008		29.19 (21.94, 38.00)	NK
20	Subtotal (I^2 = .%, p = .)		13.33 (9.72, 16.95)	
21			10.00 (0.12, 10.00)	
22	Cesarean delivery			
23	Miller, 2016		6.06 (3.85, 9.08)	NK
24	Schiff, 2005		■ 309.52 (213.14, 419.80)	
24				
26	Schiff, 2005		249.19 (201.95, 301.31)	
20 27	Schiff, 2005		262.09 (219.27, 308.53)	
	Schiff, 2010		259.26 (244.48, 274.46)	
28	Vivian-Taylor, 2012		260.14 (241.13, 279.85)	
29	Wolf, 1993	-#-	171.68 (157.35, 186.76)	NK
30	Subtotal (I^2 = 99.7%, p = 0.00		215.33 (97.40, 333.26)	
31				
32	Labor induction			
33	Schiff, 2005	·	154.76 (85.06, 250.10)	severe
34	Schiff, 2005	·	229.77 (184.04, 280.77)	
35	Schiff, 2005	·	213.74 (174.23, 257.63)	
36	Schiff, 2010		286.14 (270.87, 301.78)	
37	Subtotal (I <sup>2</sup> = 87.0%, p = 0.00		228.25 (173.87, 282.63)	i i i i i i i i i i i i i i i i i i i
38	Subtotal (1 $2 = 07.070, p = 0.00$		220.23 (173.07, 202.03)	
39	Maternal death	1 Contraction of the second		
40		I see a second se		NUZ
41	Azar, 2005	The second s	6.57 (4.68, 8.97)	NK
42	Kvarnstrand, 2008	The second s	6.61 (3.70, 10.88)	mild-severe
43	Miller, 2016	The second s	0.26 (0.01, 1.47)	NK
44	Subtotal (I^2 = .%, p = .) 🚺	The second s	4.34 (-0.72, 9.41)	
45		The second s		
46	Premature Rupture of Membranes	The second s		
47	Schiff, 2005	I see a second se	11.90 (0.30, 64.55)	severe
48	Schiff, 2005		22.65 (9.16, 46.12)	mild
49	Schiff, 2005		20.36 (8.83, 39.71)	mild-severe
50	Vladutiu, 2013a		23.53 (21.66, 25.51)	NK
51	Whitehead, 2013		95.72 (76.16, 118.34)	NK
52	Subtotal (I <sup>2</sup> = 91.8%, p = 0.00		34.09 (13.89, 54.29)	
53	Custotal (1 2 01.070, p 0.00		01.00 (10.00, 04.20)	
54	Heterogeneity between groups: p = 0.000			
55			75 74 (60 25 02 24)	
55 56	Overall (I^2 = 99.45%, p = 0.00;	Ý	75.74 (68.25, 83.24)	
57 . 58				
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	Study	ES (95% CI) Trauma
	Fetal death	
	Kvarnstrand, 2008	11.89 (7.85, 17.26) mild-sev
	Schiff, 2010	4.18 (2.29, 7.01) mild
	Wolf, 1993	3.47 (1.59, 6.58) NK
	Subtotal (I^2 = .%, p = .)	5.98 (2.16, 9.79)
	Fetal distress	
	Schiff, 2005	202.38 (122.54, 304.14) severe
	Schiff, 2005	119.74 (85.73, 161.25) mild
	Schiff, 2005	137.40 (104.94, 175.45) mild-sev
		· · · · · ·
	Schiff, 2010	50.48 (43.31, 58.44) mild
	Subtotal (I^2 = 93.6%, p = 0.00)	119.86 (57.95, 181.77)
	Meconium at delivery	
	Schiff, 2005	59.52 (19.61, 133.47) severe
	Schiff, 2005	48.54 (27.42, 78.80) mild
	Schiff, 2005	50.89 (31.36, 77.50) mild-sev
	Schiff, 2010 🖷	51.08 (43.86, 59.08) mild
	Subtotal (I^2 = 0.0%, p = 0.99)	51.01 (44.30, 57.71)
	Perinatal death	
	Kvarnstrand, 2008	101.50 (67.96, 144.24) severe
	Kvarnstrand, 2008	8.93 (4.77, 15.23) mild
	Kvarnstrand, 2008	17.62 (12.62, 23.92) mild-sev
	Hyde, 2003	5.01 (3.66, 6.70) NK
	•	
	Miller, 2016	0.79 (0.16, 2.31) NK
	Schiff, 2005	23.81 (2.90, 83.37) severe
	Schiff, 2005	16.18 (5.27, 37.36) mild
	Schiff, 2005	17.81 (7.19, 36.35) mild-sev
	Vivian-Taylor, 2012	16.82 (11.67, 23.42) mild-sev
	Vladutiu, 2013a	5.25 (4.38, 6.23) NK
	Schiff, 2010	4.18 (2.29, 7.01) mild
	Wolf, 1993	3.47 (1.59, 6.58) NK
	Subtotal (I^2 = 92.3%, p = 0.00)	8.06 (5.36, 10.76)
	Preterm delivery	
	Schiff, 2005	130.95 (67.22, 222.24) severe
		· · ·
	Schiff, 2005	245.95 (198.96, 297.89) mild
	Schiff, 2005	221.37 (181.29, 265.71) mild-sev
	Schiff, 2010	97.37 (87.53, 107.92) mild
	Vivian-Taylor, 2012	83.09 (71.42, 95.98) mild-sev
	Vladutiu, 2013a	110.33 (106.43, 114.33) NK
	Whitehead, 2013	435.77 (400.94, 471.07) NK
	Subtotal (I <sup>2</sup> = 98.6%, p = 0.00)	187.07 (141.39, 232.74)
	Respiratory distress syndrome	
	Schiff, 2005	50 52 (10 61 122 47) covere
		59.52 (19.61, 133.47) severe
	Schiff, 2005	22.65 (9.16, 46.12) mild
	Schiff, 2005	30.53 (15.88, 52.73) mild-sev
	Schiff, 2010	14.64 (10.85, 19.30) mild
	Wolf, 1993	6.17 (3.53, 10.00) NK
	Subtotal $(I^2 = 82.4\%, p = 0.00)$	16.56 (7.94, 25.19)
		10.00 (1.07, 20.13)
	Heterogeneity between groups: p = 0.000	
	Overall (I^2 = 99.27%, p = 0.00);	49.67 (42.57, 56.76)
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Outcome	Total sample size	Incidence estimate per 1,000 women (95%CI)
Maternal outcomes		
Placental problems	235329	100.00 (98.79, 101.22)
Miscarriage	3794	1.85 (0.74, 3.80)
Antepartum haemorrhage	2022	47.48 (38.62, 57.67)
Postpartum haemorrhage	2022	77.65 (66.35, 90.18)
Vaginal bleeding	235329	247.00 (245.26, 248.75)
Hospital stay >=6 days	5936	117.92 (109.82, 126.40)
Maternal death or hospitalisation	32810	135.05 (131.37, 138.80)
Fetal and neonatal		
Нурохіа	582	22.34 (11.95, 37.89)
Neonatal death	2270	5.73 (3.05, 9.77)
Neonatal transfer	2022	42.53 (34.16, 52.26

Appendix 5. Incidence of maternal, fetal & neonatal complications from single studies

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Appendix 6. Incidence in non-population level data

Outcome	Study ID	Number of events	Group size	Trauma severity level
Admission to hospital	Brookfield, 2013	182	256	Not given
	Chibber, 2015	648	728	Not given
Caesarean delivery	Chibber, 2015	529	728	Not given
	Luley 2013	32	126	Not given
	Orji, 2002	2	84	Not given
Fetal death	Aboutanos, 2007	1	148	Not given
	Chibber, 2015	78	728	Not given
Fetal distress	Chibber, 2015	412	728	Not given
Fetal tachycardia	Orji, 2002	10	84	Not given
Hydrops fetalis	Aboutanos, 2007	1	148	Not given
Maternal death	Aboutanos, 2007	0	148	Not given
	Baerga-Varela, 2000	1	39	Severe
	Brookfield, 2013	7	256	Not given
	Chibber, 2015	100	728	Not given
Maternal death	Orji, 2002	2	84	Not given
Miscarriage	Aboutanos, 2007	5	148	Not given
	Baerga-Varela, 2000	7	39	Mild to severe
Perinatal death	Baerga-Varela, 2000	23	39	Mild to severe
	Luley 2013	6	126	Not given
	Orji, 2002	3	84	Not given
Placental abruption	Chibber, 2015	428	728	Not given
	Luley 2013	7	126	Not given
	Orji, 2002	1	84	Not given
Preterm delivery	Chibber, 2015	97	728	Not given
Uterine rupture	Chibber, 2015	12	728	Not given
	Orji, 2002	1	84	Not given

## PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #			
TITLE						
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1			
ABSTRACT						
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	2-3			
INTRODUCTION						
Rationale	3	Describe the rationale for the review in the context of what is already known.	4			
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	5			
METHODS						
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	5			
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, anguage, publication status) used as criteria for eligibility, giving rationale.				
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	5			
Search	earch 8 Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.					
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	5			
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	6			
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	5-7			
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	8			
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	8			
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I <sup>2</sup> ) for each meta-analysis. For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml	8			

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### **PRISMA 2009 Checklist**

Section/topic	#	Checklist item	Reported on page #						
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).							
Additional analyses	16	ribe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating h were pre-specified.							
RESULTS									
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	9						
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	9						
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	-						
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	9						
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	10						
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).							
Additional analysis	s 23 Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]). 10								
DISCUSSION									
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	11						
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	11						
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	13						
FUNDING									
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	3						

41 From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(7): e1000097. 42 doi:10.1371/journal.pmed1000097

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# **BMJ Open**

#### Maternal trauma due to motor vehicle crashes and pregnancy outcomes: A systematic review and metaanalysis

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Date Submitted by the Author:	03-Apr-2020
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<b>Primary Subject Heading</b> :	Public health
Secondary Subject Heading:	Obstetrics and gynaecology, Medical publishing and peer review
Keywords:	ACCIDENT & EMERGENCY MEDICINE, EPIDEMIOLOGY, OBSTETRICS

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3 4	1	Maternal trauma due to motor vehicle crashes and pregnancy outcomes: A systematic review
4 5	2	and meta-analysis
6 7	3	
8	4	Amezcua-Prieto C <sup>1,2,3</sup> , Ross J <sup>4</sup> , Rogozińska E, <sup>5,6</sup> Mighiu P <sup>5</sup> , Martínez-Ruiz V <sup>1,2,3</sup> , Brohi K <sup>4</sup> , Bueno-
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Abstract

**Objectives** 

Design

maternal and offspring outcomes.

1 2

To systematically review and quantify the effect of motor vehicle crashes (MVC) in pregnancy on

Systematic review and meta-analysis of observational data searched from inception until July 1, 2018.

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women).

34 Searching was from June to August 2018 in Medline, Embase, Web of Science, Scopus, LILACS 35 SciELO, TRANSPORT, IRRD, TRANSDOC, CDSR, and Cochrane Central Register CENTRAL. 36 **Participants** Studies were selected if they focused on the effects of exposure MVC during pregnancy vs. non-37 exposure, with follow up to verify outcomes in various settings, including secondary care, collision 38 39 and emergency, and inpatient care. 40 **Data synthesis** 41 For incidence data, we calculated a pooled estimate per 1,000 women. For comparison of outcomes 42 between women involved and those not involved in MVC, we calculated odds ratios with 95% 43 confidence intervals. Where possible, we statistically pooled the data using the random-effects model. The quality of studies used in the comparative analysis was assessed with Newcastle-Ottawa Scale. 44 **Results** 45 We included 19 studies (3,222,066 women) of which the majority was carried out in high-income 46 countries (18/19). In population-level studies of women involved in MVC, maternal death occurred in 47 3.6 per 1,000 (95% CI 0.25 to 10.42; 3 studies, 12,000 women; Tau= 1.77), and fetal death or 48 stillbirth in 6.6 per 1,000 (95% CI 3.81 to 10.12; 8 studies, 47,992 women; I<sup>2</sup>=92.6%). Pooled 49 incidence of complications per 1,000 women involved in MVC was labour induction (276.43), 50 51 preterm delivery (191.90) and caesarean section (166.65). Compared to women not involved in MVC, those involved had increased odds of placental abruption (OR 1.43, 95% CI 1.27 to 1.63; 3 studies, 52 1,500,825 women) and maternal death (OR 202.27; 95% CI 110.60 to 369.95; 1 study, 1,094,559 53

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55	Conclusion: Pregnant women involved in MVC were at higher risk of maternal death and
56	complications than those not involved.
57	PROSPERO registration: CRD42018100788
58	Key terms: Pregnancy; motor vehicle crashes; pregnancy complications
59	Word count: 300
60	Strengths and limitations of this study
61	• This is the first systematic review examining the link between involvement in MVC,
62	mortality and adverse outcomes that includes evaluation of study quality assessment.
63	• This is the second systematic review looking at outcomes following MVC in pregnancy.
64	• We conducted our review using a prospectively registered protocol and reported it in
65	accordance with the international standards.
66	• Outcomes variables correspond to any trimester, not to specific trimesters.
67	• Outcomes according to seatbelt use are scarce, since only two studies use population-level
68	data.

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- 70 This research received no specific grant from any funding agency in the public, commercial
- 71 or not-for-profit sectors.
- 72 Competing interest's statement
  - 73 There are non-financial associations that may be relevant to the submitted manuscript.

#### 75 Introduction

Up to half of all women in developed countries drive motor vehicles (1) and the consequences of road traffic-related injuries involving pregnant women can be severe (2). Indeed, motor vehicle crashes (MVC) are the most common cause of non-obstetric trauma associated with fetal deaths (2.3 per 100,000 live births) (3). The risk of adverse outcomes resulting from an MVC increases in the second trimester of pregnancy if the pregnant women were the driver (4); however, this does not appear to be the case for pregnant passengers or pedestrians (5). A maternal mortality rate of 3.5 women per 100,000 is reported following MVCs in pregnant women (6). Mechanisms of injury recorded within the pregnant population of the UK national trauma registry, the Trauma Audit and Research Network (TARN), saw an increased rate of vehicular collision in pregnant women when compared to the non-pregnant cohort (7). In 2001-2008, 2.9% of pregnant women in North Carolina were drivers in one or more crashes (8). In the USA, data from the National Automotive Sampling System (NASS/CDS) reflects that when vehicles with pregnant women are involved in collision, 50% of those women will sustain an injury (9). There are few safety guidelines on travelling by car during pregnancy (10-12). The focus of these tends to be on questions around the use of seatbelts and the activation of airbags in the car (12).

There is a reported association between MVC and maternal mortality (13). Moreover, further associations such as the trigger for immediate delivery or being more likely to die are reported with severe blunt injury (Injury Severity Score (ISS) of 9 or above, or systolic blood pressure (SBP) <90mmHg on arrival) (14). Involvement in MVC is also associated with perinatal mortality (15), injuries to the abdominal region (16), placental abruption secondary to increased intra-abdominal pressure (17), preterm birth, and caesarean section (6). However, more data are required in relation to areas such as fetal outcomes and higher risk pregnancies, particularly regarding sociodemographic characteristics of the mother, specific trimester of pregnancy when exposed to trauma, socioeconomic country conditions, severity and type of trauma, and collision characteristics such as speed. A systematic review on trauma in pregnancy (including five studies reporting complications of

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involvement in MVC, and fourteen other studies on others form of trauma) showed that MVC and domestic violence were the most common causes of traumatic injury during pregnancy (4). No quality assessment of the included studies was reported in this review. Previous non-systematic reviews have published strategies used to monitor women and fetuses after a crash (18-21). However, to our knowledge there is no systematic review or meta-analysis focused on the maternal and fetal outcomes after MVC in pregnancy.

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110 *Review objectives* 

111 As the clinical impact on the mother and fetus after MVC has not been well documented, we 112 conducted a systematic review of the effect on maternal and fetal outcomes of MVC in pregnant 113 women, compared to those not involved in a collision.

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#### 115 Methods

We conducted a systematic review and reported it according to recommended standards (22). The
review was prospectively registered with PROSPERO (no. CRD42018100788).

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119 *Literature search* 

120 Searching was from June to August 2018. The following databases were used to identify relevant 121 literature: Medline, Embase, Web of Science, Scopus, LILACS (Latin-American and Caribbean System on Health Sciences Information), Science Citation Index, SciELO (Scientific Electronic 122 Library Online), TRANSPORT, IRRD (International Road Research Documentation), TRANSDOC 123 (European Conference of Ministers of Transportation databases), Cochrane Database of Systematic 124 Reviews (CDSR), and Cochrane Central Register of Controlled Trials (CENTRAL). We also sought 125 to identify unpublished research or research reported in the grey literature by searching a range of 126 relevant databases, including the Inside Conferences, Systems for Information on Grey Literature 127 128 (SIGLE) and Dissertation Abstracts. Furthermore, the searches of the medical database were supplemented with the Internet search using a general search engine (e.g. Google, 129 www.google.co.uk/) and safetylit.org. Language and date restrictions were not applied to electronic 130

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131 searches. Relevant studies were identified using a combination of, but not limited to, the medical subject headings (MeSH) and keywords for "motor vehicle collision" (OR road traffic collision OR 132 crash OR collision) and "pregnancy" (OR pregnant women OR gravid women OR childbearing 133 134 women OR maternal).

136 *Review inclusion criteria* 

137 Papers were selected if they studied the effects of exposure to trauma due to involvement in an MVC 138 during pregnancy vs. non-exposure, with follow up to verify outcomes in various settings including 139 secondary care, collision and emergency, and inpatient care. Observational studies (cohort studies, case-control design, non-intervention arms of randomised controlled trials) were included. Case series 140 and case reports were excluded. Appendix 1 shows the search strategy for Medline (via Ovid) and 141 Appendix 2 the excluded studies with reasons. 142

#### 144 Data extraction and study quality assessment

A double screening of papers was carried out. Two reviewers (CAP & JR) independently extracted 145 the relevant data from each full-text article and data were recorded using a standardized data 146 147 extraction form. A data extraction form was piloted for each study design and amended as required. Discrepancies were resolved by consensus or by a discussion with a third senior author (ER). We 148 extracted data on a) severe adverse maternal outcomes such as maternal death, miscarriage and 149 preterm birth (<37/40 and <34/40); b) severe adverse fetal outcomes such as intrauterine 150 death/stillbirth and neonatal death. Secondary outcomes were: a) individual components of maternal 151 outcomes such as preterm labour, mode of delivery (vaginal delivery vs caesarean section), premature 152 rupture of membranes (PROM), preterm premature rupture of membranes (PPROM), placental 153 abruption, chorioamnionitis/sepsis and maternal admission to an intensive care unit (ICU) or high 154 155 dependency unit (HDU); b) individual components of fetal outcomes: respiratory distress syndrome, neonatal ICU admission, low birth weight (LBW) and small for gestational age (SGA). 156

We also extracted data on 1) adverse outcomes in pregnant women involved in MVC and their offspring in subgroups according to maternal characteristics (low, high and any risk), trimester of exposure, country (low and middle income, high income), type of trauma (penetrating, blunt, burns), severity of trauma (mild, moderate, severe), seatbelt use (yes, no), study quality (low, high); 2) risk factors for pregnancy complications following MVC such as maternal characteristics (age, parity, high risk pregnancy, gestational age), type of trauma, type of motor vehicle, type of collision, collision characteristic (stationary, high or moderate speed) and seat belt use.

The quality assessment of studies was independently evaluated by two reviewers (JR and CAP) using the Newcastle-Ottawa Scale (23). This scale includes 8 items, 4 items about selection criteria of cases or cohorts in case-control or cohort designs, respectively; 2 items about comparability between groups (in both designs); and 3 items about exposure criteria in case-control designs and about outcomes in cohort designs. Any of those studies could be awarded a maximum of one star for each numbered item within the selection and exposure categories. A maximum of two stars could be given for comparability. For the incidence analysis, we considered six aspects (24): 1) representativeness of cohort; 2) design; 3) method of sampling; 4) adequacy of follow-up; 5) if the outcomes were adequately ascertained and 4) if measurement or misclassification bias were minimized. Studies without these features or with unclear reporting were classified to have a high risk of bias. 

176 Patient and Public Involvement

177 "No patient involved"

178 Data synthesis

We undertook random-effects meta-analysis to determine the odds ratios (OR) with 95% confidence intervals (CI) for maternal and offspring complications from MVC. We estimated heterogeneity between the included studies with Chi-Square test of Q (I2) excepting when not enough studies were in the meta-analysis (2-3), and we pooled the rates of maternal/fetal complications and reported with 95% CI. For each primary outcome, a meta-analysis was conducted for studies sufficiently homogeneous in terms of the characteristics of participants and exposure. The subgroup analysis was applied in: a) trimester of pregnancy during which the trauma occurred; b) maternal risk status (low, Page 9 of 38

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high, any risk); c) type of trauma; d) severity of trauma (using the ISS to categorize the severity of
trauma sustained following MVC) (25); e) setting (low and middle income, high-income country); f)
year of study publication: (before or after the introduction of mandatory seatbelt legislature in the
country of study); and g) study quality according to the Newcastle and Ottawa Scale (23).

191 Results

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192 Study selection

193 Out of 1,739 retrieved references, 19 studies met the eligibility criteria (Figure 1). Five of these 194 reported data allowing us to compare pregnancy complications between pregnant women involved in 195 MVC and those not involved in MVC (6, 26-29). The totality of the studies (n = 19) contributed to the 196 analysis of the incidence of pregnancy complications among women involved in MVC (6, 17, 26-42).

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#### 198 *Characteristics of included studies*

The characteristics of included studies are in Table 1. Included studies were published between 1993 199 and 2016. Most of them were carried out in developed, high-income countries such as USA (14/18) 200 201 (26, 28-31, 33-41), Sweden (1/19) (27), Kuwait (1/19) (17) and Israel (1/19) (42). The number of included pregnant women varies, ranging from 39 to 1,094,559. The data was sourced from hospital 202 records/trauma registries (7/19) (17, 31, 32, 35, 38, 39, 42) or from population-level databases (12/19) 203 (6, 26-30, 33, 34, 36, 37, 40, 41). The majority of studies collected information on outcomes of 204 205 pregnant women involved in MVC during any trimester of pregnancy. 8 out of 19 studies reported 206 information about the use of safety devices such as seatbelts and/or airbag (26, 29, 30, 33, 35, 37-39). 207 Also in eight studies, the authors assessed the severity of MVC injuries with five of these using a 208 validated tool (28, 31, 35, 38, 42) – most of them reporting ISS (28, 31, 35, 42) and one the Revised 209 Trauma Scale (38).

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211 Quality assessment

212 60% of studies had a low risk of bias with regards to the adequacy of representativeness and random
213 sample selection (12/19). None of the studies was prospective. The categories of follow up of more

than 80% of participants, outcome ascertainment and misclassification bias showed low risk (Figure
2). The five papers included for comparison of complication rates between pregnant women exposed
to MVC and those who were not exposed (assessed using the Newcastle-Ottawa Scale) showed
generally high quality, with four papers scoring 9/9 (6, 26, 28, 29). The remaining paper scored 8/9,
losing one point for the comparability as it did not control for any secondary factors (27).

#### 220 Incidence of complications among pregnant women involved in motor vehicle crashes

The assessment of adverse outcome incidence among women involved in MVC (using population-level data) demonstrated incidence estimations of 276.43 per 1000 for induction of labour (95% CI 262.54 to 290.54), 191.90 per 1000 for preterm delivery (95% CI 45.98 to 405.74), and 166.65 per 1000 for caesarean section (95% CI 47.34 to 339.00). The estimated incidence rates for other complications included 42.33 per 1000 for PROM, 17.08 per 1000 requiring admission to hospital, 16.14 per 1000 for placental abruption and 15.19 per 1000 for neonatal respiratory distress. A pooled incidence of maternal death was 3.60 per 1000 women (95% CI 0.25 to 10.42, 3 studies, 12,000 women, Tau=1.77). The pooled incidence of perinatal death (fetal death or stillbirth) per 1000 women was 6.60, (95% CI 3.81 to 10.12; 8 studies, 47,992 women; I<sup>2</sup>=92.6%) (Table 2). The representation of the maternal and offspring outcomes according to trauma severity are in appendices (Appendices 3 and 4). Using data from single hospital centres, the random pooled estimation for the incidence of admission to hospital was 117.92 per 1000 women (95% CI 109.82 to 126.40) (17, 38); for maternal death was 135.05 per 1000 women (95% CI 131.37 to 138.80) and for fetal death was 5.73 per 1000 women (95% CI 3.05 to 9.77) (Appendices 5 and 6).

#### 236 Pregnancy complications in women involved vs not involved in motor vehicle crashes

We observed a statistically significant link between involvement in MVC and maternal death (OR 202.3, 95% CI 110.60 to 370.00; single study) (27) (data not shown in table or graphic). Figure 3 shows pooled results from population-level data, demonstrating a positive association between MVC and placental abruption (OR 1.43 95% CI 1.27 to 1.63). Two studies contributed data used in sensitivity analyses stratifying by seatbelt use, where the pooled estimation (26, 29) of fetal death

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decreased with seatbelt devices, but the association was not statistically significant (OR 0.66 95% CI 0.36 to 1.19) (Figure 1, supplementary). The review manager forest plot displays a positive but not statistically significant association between fetal death and MVC without seatbelt use (OR 5.78 95% CI 0.17 to 201.12, Tau<sup>2</sup> = 6.51) (Figure 2, supplementary).

#### 247 Discussion

#### 248 Statement of principal findings

This review estimated that for women involved in MVC, maternal death occurrence was 3.6 per 1000 and perinatal death 6.6 per 1000 women. Compared to women not involved in MVC, those involved had an increased odds of placental abruption, antepartum haemorrhage and maternal death. The pooled incidence of complications per 1,000 women involved in MVC was, from the higher incidence to the lower, induction of labour, preterm delivery, caesarean section, premature rupture of membrane, and placental abruption (population level-data).

#### 256 Strengths and weaknesses of this study

This is the second systematic review, after the one of Mendez Figueroa et al., in 2013 (4), looking at outcomes following MVC in pregnancy. We conducted our review using a prospectively registered protocol (PROSPERO) and reported it in accordance with the international standards (43). This review, to our best knowledge, is the first one examining the link between involvement in MVC, mortality and adverse outcomes that involves evaluation of study quality assessment; 14 studies looking at outcome incidence related to MVC (17, 30-42) and 5 studies comparing outcomes in pregnant women involved in MVC and those who were not (6, 26-29). We used established tools to assess outcome reporting quality for the incidence rates (44) and comparability (45). We included data from population-level and single centre studies, but the analysis and reporting of the results were independent in order to get precision and validity in the estimations. However, a couple of graphics of the maternal and offspring's outcomes incidences have been included as Appendix 3 and 4. Between August 2018 and March 2020, there have been no new studies eligible to include in the systematic review.

For the incidence analysis, we evaluated the quality of the 19 studies of this systematic review. The highest risk was in the design. None of the studies had a prospective design. The representativeness of cohort and the random method of sampling were other limitations of the quality of studies, with 7 out of 19 studies having a high risk of bias in these areas (17, 31, 32, 35, 38, 39, 42). However, the quality assessment of the five papers included for comparison of complication rates between pregnant women involved and not involved in MVC using the Newcastle-Ottawa Scale showed generally high quality, with four papers scoring 9/9 (6, 26, 28, 29).

The weaknesses of this systematic review are as follows. Firstly, outcomes were not reported by trimester, with 13 out of 19 papers focused on MVC at any trimester. Secondly, outcomes, according to seatbelt use, are scarce as only two studies using population-level data looked at safety features as a stratification factor (26, 29). Two studies with data sourced from hospital records/single-site trauma registries (38, 39) and three studies utilising population-level databases (26, 29, 30) reported some outcomes regarding seatbelt-use. Thirdly, we found a limited number of relevant studies comparing outcomes between women involved and not involved in MVC. The majority of the studies were carried out in the USA (26, 28, 29) with most recent one published in 2013 (29). Fourthly, the included studies differed in study design with seven of them using hospital records/single-site trauma registry (17, 31, 32, 35, 38, 39, 42) and twelve population database (6, 26-30, 33, 34, 36, 37, 40, 41). Despite analysing the data within the respective study designs and incorporation of anticipated variation into the statistical model (random-effects) (46), we encountered substantial statistical heterogeneity in the pooled estimates that could not be formally explored due to a limited number of studies and poor reporting of important factors such as trauma severity. As a fifth point, these data apply to developed countries - only one of the papers included data from an underdeveloped country, perhaps influencing the outcomes that might otherwise be seen in the developed world. Finally, in only eight studies did authors assess severity of MVC injuries, with only five of these using a validated tool (28, 31, 35, 38, 42). This was a challenge when aiming to analyse results according to the severity of the crash.

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3 4	298	
5 6	299	Meaning of the study
7 8	300	The strongest association was found between placental abruption (6, 28, 29) and MVC. Maternal
9 10	301	death was associated with involvement in MVC but this finding needs to be treated with caution as the
11 12	302	data come from a single study (27). The outcomes in descending order of incidence estimate per 1000
13 14	303	(population-level data) were the induction of labour, preterm delivery, caesarean section, premature
15 16 17	304	rupture of membranes, and admission to hospital, placental abruption and maternal death. In the
17 18 19	305	analyses stratified by use of seatbelt, we observed an association of fetal death with lack of seatbelt
20 21	306	use by pregnant women involved in an MVC. However, this finding was not statistically significant
22 23	307	and informed by a limited number of studies. Previous studies have shown that pregnant women
24 25	308	wearing seatbelt during the MVC did not experience a significantly higher risk of adverse fetal
26 27	309	outcomes than women who were not involved in MVC (47) Furthermore, airbags seem to be
28 29	310	contributing to the protection of both pregnant drivers and their fetuses (48).
30 31	311	The results of this systematic review provide evidence informing primary prevention measures,
32 33	312	recommendations and educational interventions for pregnant women in the context of MVC that
34 35	313	should be incorporated into the primary care guidelines.
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38 39 40	315	Unanswered questions and future research
40 41 42	316	The effects of MVC in pregnant women is a specific field that requires further research and an
43 44	317	improved methodological approach to determine the risks of adverse maternal and fetal outcomes.
45 46	318	Additional variables such as trauma severity, the position of the women in the car, use of seatbelt,
47 48	319	deployment or non-deployment of an airbag, severity of the crash and gestational week of pregnancy
49 50	320	should be recorded in relation to MVC exposure in order to allow more precision when analysing
51 52	321	outcomes. A greater number of well-designed studies in a variety of global settings would strengthen
53 54	322	current evidence-base.
55 56 57	323	
57 58 59 60	324	Conclusions

Pregnant women involved in MVC seem to be at increased risk of maternal death and complications, especially placental abruption, than those not involved in MVC. The risk of complications such as preterm delivery, premature rupture of membranes and caesarean section were also increased. However, these findings need to be treated with caution due to considerable between study differences. Road traffic authorities should be conscious and strict in targeting preventive measures aimed at pregnant users of motor vehicles due to risk associated with potential involvement in MVC. Word count: 3,137

**Author's contribution** 

PM conducted literature searches and screened publications jointly with JR. CAP and JR extracted the data. CAP and ER drafted the manuscript and conducted the statistical analyses. KSK and ST designed the study review. CAP is the guarantor. Authors VMR, KB, ABC, ST and KSK gave critical revision of the manuscript. All authors had full access to the data and take responsibility for the data analyses.

The corresponding author attests that all listed authors meet authorship criteria.

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Universities.

#### **Data sharing Statement**

Data have been extracted for original papers. Dataset generated has been used for the meta-analyses.

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#### Table 1. Characteristics of included studies

Study ID Author, year, Country	Design	Sample size	Time period	Inclusion criteria	Data source	Trimest er	Seatbelt use (with data)	Assessment of trauma severity (with data)	Method of assessing trauma severity	Maternal outcomes	Offspring outcomes
Population-leve	el data										
<b>Azar, 2005</b> USA	population-based matched retrospective cohort (incidence only)	5936	2003- 2011	Admitted to hospital following MVC while pregnant	Population-based cohort	any	no	no	N/A	Maternal death	
<b>Hyde, 2003</b> USA	retrospective cohort (incidence and comparison)	322704	1992- 1999	Pregnant drivers involved in MVC	Linked databases (police registry & birth/death certificates)	any	yes	yes	Study- specific definition <sup>1</sup>		Fetal death
<b>Kvarnstrand,</b> 2008 Sweden	retrospective cohort (incidence and comparison)	1094559	1991- 2001	Maternal inclusion on the accident register > 28 GW	Linked databases (police registry & birth/death certificates)	2 <sup>nd</sup>	no	yes	Study specific definition <sup>2</sup>	Maternal death	Fetal/neonatal death
<b>Kuo, 2007</b> JSA	retrospective chart/database review (incidence only)	16982 injuries 4479 (in MVC)	2002	Pregnant women hospitalized with injury (only MVC used)	Sample from population level cohort (National Inpatient Sample)	any	no	no	N/A	Delivery, hospitalization	
Schiff, 2005 JSA	retrospective cohort (incidence and comparison)	17899	1989- 2001	Hospitalized for MVC and with a singleton livebirth or fetal death	Linked databases (hospital discharge data & birth/death certificates)	any	no	yes	ISS	Preterm birth, PROM, C-section, placental abruption	Stillbirth LBW, SGA, Fetal distress, RDS, Meconium
Schiff, 2010 JSA	retrospective cohort (incidence only)	3348	2002- 2005	Nonrollover MVC among pregnant front seat occupants	Linked databases (hospital discharge data & birth/death certificates)	any	yes (airbag) no (seatbelt)	no	N/A	Preterm birth, placental abruption, labour induction, C- section	Stillbirth, LBW SGA, RDS Fetal distress Meconium
7 <b>ivian-</b> T <b>aylor, 2012</b> Australia	retrospective cohort (incidence and comparison)	604380	2000- 2007	Women who gave birth exposed and not exposed to MVC	Linked databases (hospital discharge data & birth/death certificates)	2 <sup>nd</sup>	no	yes	Study- specific definition <sup>3</sup>	Admission, placental abruption, APH,PPH, preterm birth, C- section	Perinatal death (>20 <sup>th</sup> GW), neonatal transfer

<b>Vladutiu,</b> 2013 USA	retrospective cohort (incidence and comparison)	878546	2001- 2008	Pregnant women 16-46 years, > 20GW, delivering a live/ stillbirth singleton infant	Linked databases (police registry & birth/death certificates)	2 <sup>nd</sup>	yes (seatbelt) yes (airbag)	no	N/A	Placental abruption, PROM, preterm birth	Stillbirth
<b>Weiss, 2002</b> USA	crash database pregnant vs. non- pregnant (NASS/CDS) (incidence only)	32810	1995- 1999	Pregnant and non- pregnant women 15–39 years	Sample from population-level database of traffic accidents	any	yes	no	N/A	Maternal death	
<b>Weiss, 2008</b> USA	retrospective cohort (incidence only)	1816	1999- 2002	Injury-related emergency department visits by pregnant women (only MVC used)	Linked databases (hospital discharge data & birth/death certificates)	any	no	no	N/A	Hospital admission	
<b>Whitehead, 2013*</b> USA	PRAMS survey database (incidence only)	235329	2000- 2005	Survey of women who recently delivered a live- born infant	Population-based cohort (PRAMS)	any	no	no	N/A	Preterm birth, UTI, PROM	
<b>Wolf, 1993</b> USA	population-based retrospective cohort (incidence only)	2582	1980- 1988	Pregnant women drivers involved in MVC >20GW	Linked databases (police registry & birth/death certificates)	2 <sup>nd</sup> & 3 <sup>rd</sup>	yes	no	N/A	Preterm birth, placental abruption, C-section	Stillbirth, LBW, RDS
Single hospita	l records/trauma regi	istry									
<b>Aboutanos,</b> 2007 USA	retrospective chart/database review (incidence only)	148	2001- 2005	Pregnant women presenting to ED following MVC	Single hospital records from trauma centre	any	yes (only in miscarriage)	yes	ISS	Maternal death, miscarriage	Fetal death hydrops fetali
Baerga- Varela, 2000 USA	retrospective chart/database review (incidence only)	39	1986- 1996	Admitted to hospital after MVC while pregnant	Single hospital records	any	no	yes	ISS	Maternal death, miscarriage	Stillbirth
Brookfield, 2013 USA	retrospective chart/database review (incidence only)	256	1990- 2007	Pregnant women presenting to ED following MVC	Single hospital records from trauma centre	any	yes	yes	ISS and RTS	Maternal death, admission to hospital	

Chibber, 2015 Kuwait	retrospective chart/database review (incidence only)	728	2009- 2012	MVC, pregnant, treated at major tertiary hospitals	Single hospital records	2 <sup>nd</sup>	no	no	N/A	Maternal death, placental abruption, preterm birth, uterine rupture, C-Section,	Fetal death, fetal distress
Luley, 2013 USA	retrospective chart/database review (incidence only)	126	1994- 2010	Pregnant women after an MVC >14/40 GA	Single hospital trauma database	2 <sup>nd</sup> & 3 <sup>rd</sup>	yes	no	N/A	admission Maternal death, placental abruption, C-section	Stillbirth
Miller, 2016 Israel	(incidence only) retrospective cohort (incidence only)	3794	2006- 2013	Women 18-40 years, in MVC and hospitalized (only pregnant cohort used)	National trauma registry	any	no	no	ISS	Maternal death, miscarriage, placental abruption, C-section	Stillbirth
Orji, 2002 Nigeria	retrospective chart/database review (incidence only)	84	1980- 2000	Pregnant women in MVC managed in tertiary hospitals	Single hospital records**	any	no	no	N/A	Maternal death, placental abruption, uterine rupture, C-section	Perinatal death (fetal death), fetal tachycardia

ISS: Injury Severity Score; RTS: Revised Trauma Score; ICU: Intensive Care Unit, N/A not applicable; GA: Gestational Age; LBW: Low birth weight; SGA: Small for gestational age; RDS: Respiratory distress syndrome. \*National survey; \*\*Two hospitals in same region included; <sup>1</sup>Possible/probable/incapacitated/fatal; <sup>2</sup>Fatal/major/minor/uninjured; <sup>3</sup>'Severe' = admission to ICU and/or blood transfusion and/or injury to abdomen/pelvis/lower back.

Table 2. Incidence of adverse outcomes per 1,000 women involved in motor vehicle crashes.

Outcome and study	Number of studies	Number of women	Incidence estimate per 1,000 women	95% CI
Maternal		I		
Maternal death	3	12000	3.60	(0.25 to 10.42)
Azar, 2005			6.57	(4.68 to 8.97)
Kvarnstrand, 2008			6.61	(3.70 to 10.88)
Miller, 2016			0.26	(0.01 to 1.47)
Admission to hospital	2	3838	17.08	(13.20 to 21.46)
Vivian-Taylor, 2012			8.90	(5.28 to 14.03)
Weiss, 2008			29.19	(21.94 to 38.0)
Placenta abruption	6	36737	16.14	(7.04 to 28.78)
Wolf, 1993			8.10	(5.02 to 12.36)
Miller, 2016	9	4	1.05	(0.29 to 2.70)
Schiff, 2005		<u>_</u>	113.40	(88.80 to 142.01)
Schiff, 2010			12.25	(8.80 to 16.58)
Vivian-Taylor, 2012		4.	16.32	(11.26 to 22.84)
Vladutiu, 2013		()	7.17	(6.15 to 8.31)
Preterm delivery	5	265680	191.90	(45.98 to 405.74)
Schiff, 2005			316.15	(278.53 to 355.65)
Schiff, 2010			97.37	(87.53 to 107.92)
Vivian-Taylor, 2012			83.09	(71.42 to 95.98)
Vladutiu, 2013			110.33	(106.43 to 114.33)
Whitehead, 2013			437.00	(435.00 to 439.01)
PROM	3	260310	42.33	(5.87 to 109.24)
Schiff, 2005			22.34	(11.95 to 37.89)
Vladutiu, 2013			23.53	(21.66 to 25.51)
Whitehead, 2013			96.00	(94.81 to 97.20)
Labour induction	2	3930	276.43	(262.54 to 290.54)

Schiff, 2005			223.37	(190.15 to 259.42)
Schiff, 2010			286.14	(270.87 to 301.78)
Caesarean section	5	12338	166.65	(47.34 to 339.00)
Miller, 2016			6.06	(3.85 to 9.08)
Schiff, 2005			254.30	(219.38 to 291.73)
Schiff, 2010			259.26	(244.48 to 274.46)
Vivian-Taylor, 2012			260.14	(241.13 to 279.85)
Wolf, 1993			171.68	(157.35 to 186.76)
Offspring				
Perinatal death	8	47992	6.60	(3.81 to 10.12)
Kvarnstrand, 2008	fetal/neonatal		17.62	(12.62 to 23.92)
Hyde, 2003	fetal		5.01	(3.66 to 6.70)
Miller, 2016	stillbirth	4	0.79	(0.16 to 2.31)
Schiff, 2005	fetal		12.03	(4.85 to 24.62)
Vivian-Taylor, 2012	stillbirth	Ö,	16.82	(11.67 to 23.42)
Vladutiu, 2013	stillbirth		5.25	(4.38 to 6.23)
Schiff, 2010	fetal	(O)	4.18	(2.29 to 7.01)
Wolf, 1993	fetal		3.47	(1.59 to 6.58)
Fetal distress	2	3930	60.09	(52.85 to 67.77)
Schiff, 2005			132.30	(105.84 to 162.56)
Schiff, 2010			50.48	(43.31 to 58.44)
Meconium at delivery	2	3930	52.61	(45.82 to 59.85)
Schiff, 2005			63.57	(45.15 to 86.57)
Schiff, 2010			51.08	(43.86 to 59.08)
RDS	3	6522	15.19	(5.83 to 28.68)
Schiff, 2005			32.65	(19.77 to 50.51)
Schiff, 2010			14.64	(10.85 to 19.30)
Wolf, 1993			6.17	(3.53 to 10.00)

**Data source: population database**; CI, Confidence Interval; PROM: Premature Rupture of Membranes; RDS: Respiratory Distress Syndrome.

#### **Figures**

Figure 1. The study selection process in the systematic review of outcomes on pregnant women involved in motor vehicle crashes

Figure 2. The quality assessment of the included studies

Figure 3. Comparison of outcomes between women involved and not involved in motor vehicle crashes

Figure 1. (Supplementary). Comparison of pregnancy complications between women involved and not involved in motor vehicle crashes stratified by seatbelt use

Figure 2. (Supplementary). Comparison of fetal death between women involved and not involved in motor vehicle crashes stratified by seatbelt use

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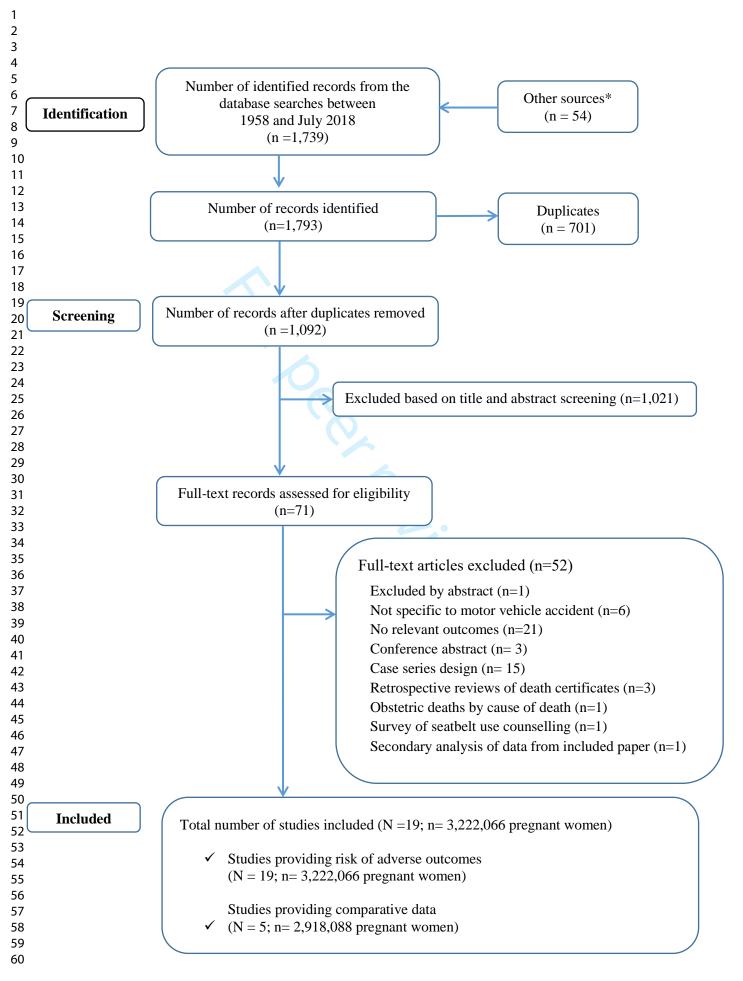
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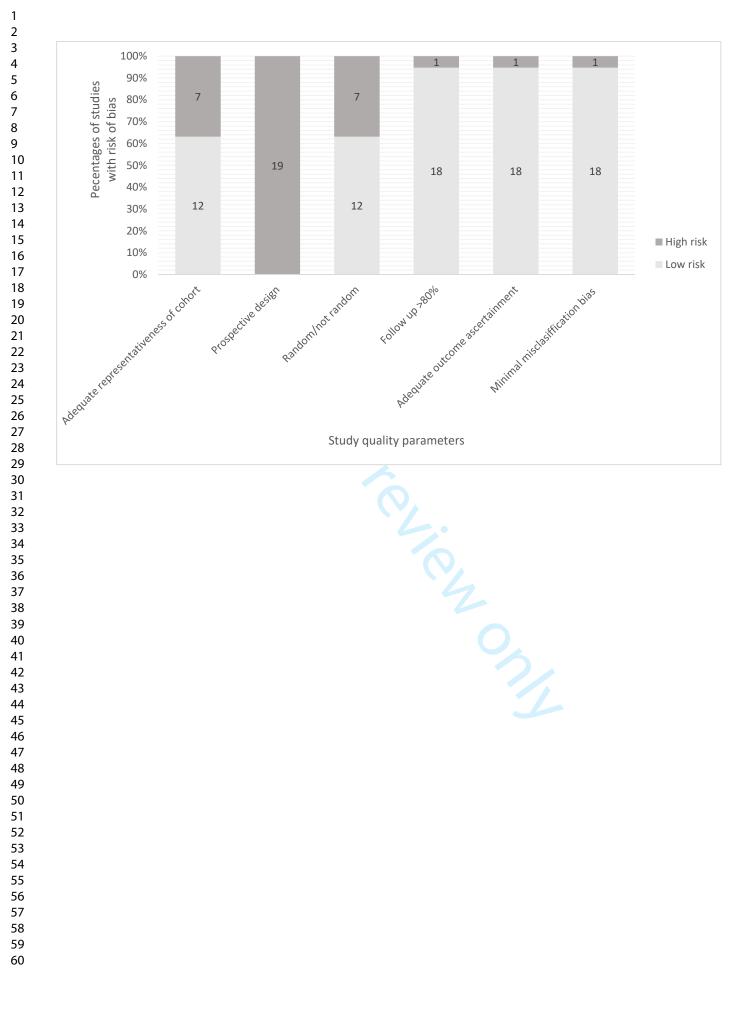
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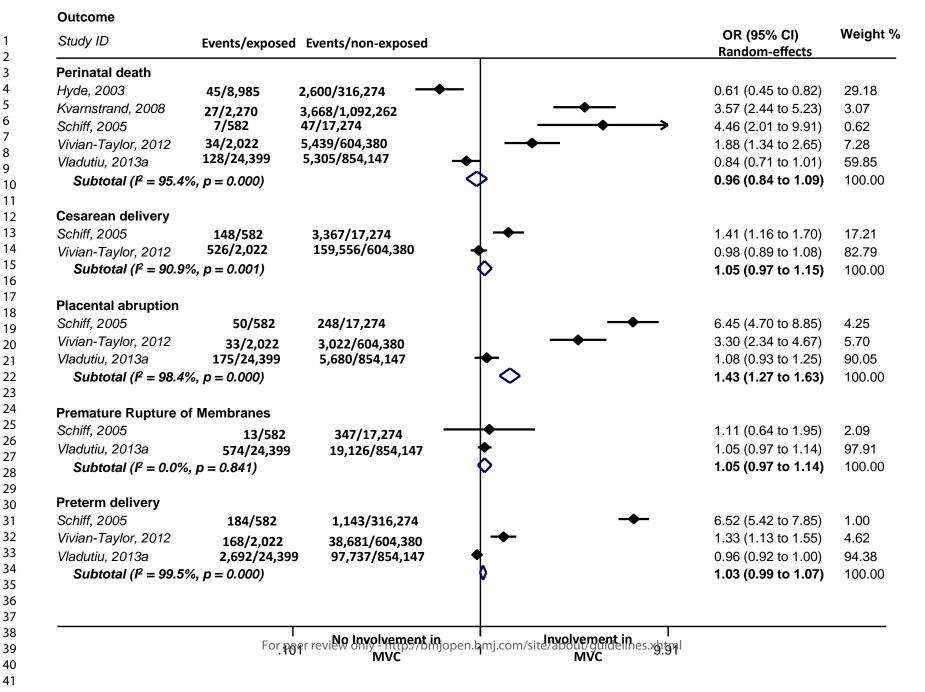
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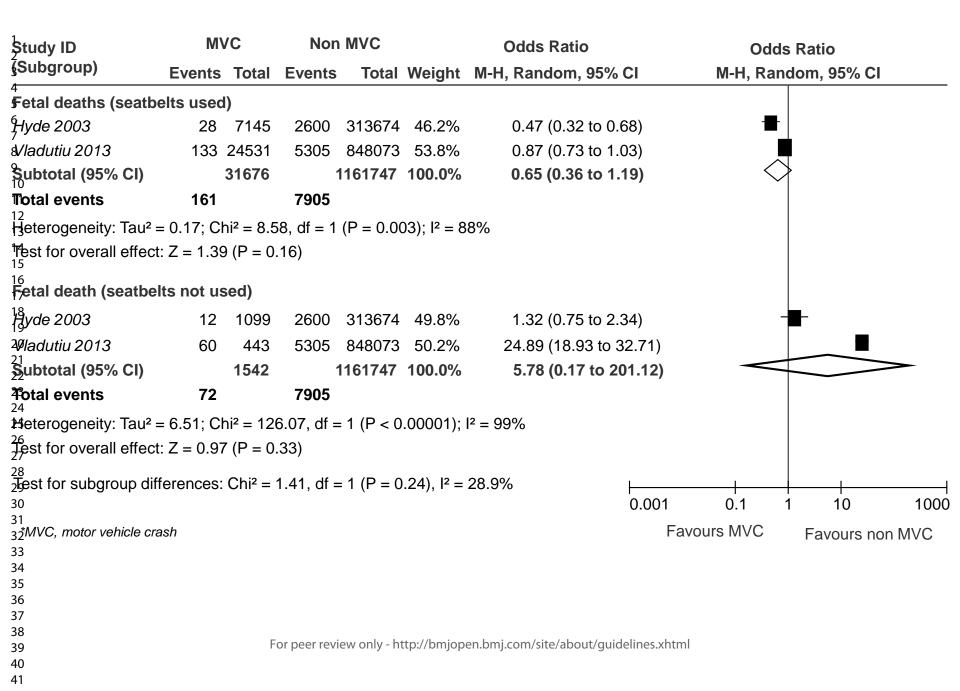


\*references of relevant non-systematic reviews and Google scholar





Page 27 of 38 Outcome					BMJ Open		
1	Study ID	Overall incidence	Study size			OR (95% CI)	
2	Fetal death						
4 5	Seatbelts not u	sed					
6	Hyde, 2003	1.176	2222			1.32 (0.74 to 2.33)	
7 8	Vladutiu, 2013a	5.333	1006			← 21.65 (16.51 to 28.39)	
9 10	Seatbelts used						
11	Hyde, 2003	.1832	14346		- <b>-</b> -	0.47 (0.33 to 0.69)	
12 13	Vladutiu, 2013a	.1102	49328		◆	0.87 (0.73 to 1.03)	
14 15		l					
16 17		sed					
18	Vladutiu, 2013a	.1152	49328	← ◆	-	0.02 (0.01 to 0.06)	
19 20							
21 22	Vladutiu, 2013a	.1188	49328		•	1.09 (0.93 to 1.26)	
23							
24 25	Seatbelts not u						
26		97.2	1006			0.85 (0.64 to 1.14)	
27 28							
29	Vladutiu, 2013a	2.035	49328		•	0.94 (0.90 to 0.97)	
30 31	Premature Rupture	Of Membran	es				
32 33		sed					
34		.388	49328			0.02 (0.01 to 0.04)	
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41				.00586	1	171	



#### BMJ Open

Item	Search term
1	pregnancy.af.
2	pregnan*.sh.
3	gravidity.sh.
4	gravid*.sh.
5	gestation*.sh.
6	pregnant women.sh.
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8	(child adj3 bearing).tw.
9	childbearing.af.
10	matern*.sh.
11	vehicle* crash*.af.
12	vehicle* accident*.af.
13	vehicle* collision*.af.
14	motor vehicle crash*.af.
15	motor vehicle accident*.af.
16	motor vehicle collision*.af.
17	motor vehicle injur*.af.
17	vehicle* injur*.af.
	road traffic crash*.af.
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20	road traffic accident*.af.
21	road traffic collision*.af.
22	road traffic injur*.af.
23	auto* crash*.af.
24	auto* accident*.af.
25	auto* collision*.af.
26	auto* injur*.af.
27	car crash*.af.
28	car accident*.af.
29	car collision*.af.
30	car injur*.af.
31	(car adj3 trauma).af.
32	(automobile adj3 trauma).af.
33	(automotive adj3 trauma).af.
34	(road traffic adj3 trauma).af.
35	(motor vehicle adj3 trauma).af.
36	1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10
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38	27 or 28 or 29 or 30 or 31 or 32 or 33 or 34 or 35 36 and 37

Appendix 1. Search strategy for MEDLINE (via Ovid) executed from database inception up to July 2018

	Appendix 2 List of	of excluded studies	with reasons
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Study ID	Reason	Reference
Al Mulhim, 2012	Pregnancy loss or not after trauma in Arabic pregnant women	EMHJ. Vol. 18 No. 5 2012
Battaloglu 2016	From a cohort of 15,140 female patients, 173 were pregnant women in the trauma registry. 55.5% of them from vehicle collision	SR Petrone, 2017 Injury, Int. J. Care Injured 47 (2016) 184-187
Barre 2006	Pregnant women with abdominal trauma during pregnancy (n=65). Half of them from a traffic accident.	<b>SR Petrone, 2017</b> La Revue Sage-Femme. Vol 5, Issue 6, 2006, 312-316
Cannada 2010	Pregnant women with orthopaedic injuries (n=65)	SR Petrone, 2017 Injury, Infection, and Critical Care.2010. Vol. 69 (3)
Chamberlain, 2011	Communication abstract. Retrospective cohort study. Identification of 272 pregnant trauma victims. 78.6% of them incurred in a MVC. No data to extract	American Journal of Obstetrics & Gynecology Supplement to January 2011
Cheng, 2012	Maternal complications during delivery according to uninjured, minor and severe injuries. 2,881 pregnant women (47,4%) involved in MVC	World J Surg (2012) 36:2767– 2775
Connolly, 1997	476 maternal records of trauma cases. 54.6% were MVC. No more data available	American Journal of Perinatology.1997.Vol. 14 (6)
Corsi 1999	Twenty-seven traumatised pregnant women were analysed retrospectively over a period of 9 years in Sao Paulo, Brazil	SR Petrone, 2017 Injury, Int. J. Care Injured 30 (1999) 239-243
Dannenberg, 1995	Homicide and other injuries as causes of maternal death between 1987 and 1991 in New York	Am J Obstet Gynecol Vol.172 (5)
Deshpande, 2017	Trauma impact on maternal mortality. Comparability between pregnant vs. non pregnant women	American Journal of Obstetrics & Gynecology 2017. 590.e2
El Kady 2004	Retrospective cohort study of women hospitalized for Trauma in California	SR Petrone, 2017 American Journal of Obstetrics and Gynecology (2004) 190, 1661-8
El Kady D, 2006	Fractures injuries on maternal/neonatal outcomes in United States	SR Méndez -Figueroa 2013 American Journal of Obstetrics and Gynecology (2006) 195, 711–6
Fischer 2011	Minor trauma and poor fetal outcomes in Tennessee, Memphis	SR Petrone, 2017 Injury, Infection, and Critical Care. 2011. Vol. 71 (1)
Gibbins, 2017	Communication. MVC and Stillbirth. Secondary analysis of 439 stillbirth	American Journal of Obstetrics & Gynecology Supplement to January 2017
Goodwin, 1990	Case-series of trauma pregnant women between 1987 and 1988 in Los Angeles	SR Méndez -Figueroa 2013 Am J Obstet Gynecol. 1990 Vol. 162 (3).
Hardt, 2013	Prenatal risk screening to identify women at increased risk for traumatic pregnancy-	Women's Health Issues 23-3 (2013) e187–e193

	associated death	
Hardy, 1974	Maternal mortality ratios at large urban	Obstetric and Gynecology.
	charity hospitals from 1941 to 1971	1974. Vol.43 (1)
Harland 2014	Risks factors of maternal injuries in a	SR Petrone, 2017
	population-based sample of pregnant women	Journal of Women's Health.
	from Iowa	2014. Vol. 23 (12)
Hitosugi 2006	135 traffic accidents involving Japanese	SR Petrone, 2017
	pregnant women from insurance companies.	Forensic Science International
	The outcomes of neonates determined by	159 (2006) 51-54
	their condition 1 month after birth	
	(death/abortion/healthy)	
Ikossi, 2005	Risks factors of trauma in pregnant women	J Am Coll Surg. Vol. 2005. 200
	from San Francisco, California	(1)
Lynch, 2011	Pregnancy associated- death in Ohio: 2003-	American Journal of Obstetric
	2007	& Gynecology Supplement to
		January 2011
Manoogian, 2015	Injuries characteristics between pregnant vs	Accident Analysis and
	non pregnant women occupants (not	Prevention 74 (2015).
	outcome)	69–76
Melamed 2012	Outcomes following blunt trauma in Pregnant	SR Petrone, 2017
	women from Israel	The Journal of Maternal-Feta
		and Neonatal Medicine. 2012
Marada abiaita 2012		25(9): 1612–1617
Mesdaghinia, 2012	Causes of trauma in 32 pregnant women with	Arch Trauma Res.
Namini 2000	trauma in a Hospital in Iran	2012;1(1):23-26
Nannini, 2008	Risks of injury in pregnant women in Massachusets	Journal of Midwifery & Women's Health.2008. Vol.53
	Massachusets	(1)
Omoke, 2013	Trauma during pregnancy in a Nigerian	Int J Crit Illn Inj Sci. 2013; 3(4)
OIII0KE, 2013	setting	269–273.
Osei-Ampofo, 2016	A cross-sectional study with 134 pregnant	African Journal of Emergency
03cl Ampolo, 2010	women from Ghana visiting the emergency	Medicine (2016) 6, 87 –93
	care. Leading injury MVC (23%). Not	
	outcomes	
Pak, 1998	Delivery outcomes after a blunt abdominal	Am J Obstet Gynecol. 1998.
,	trauma in 85 pregnant women	Vol. 179 (5)
Patteson, 2007	High risk factors involved in trauma during	The Journal of TRAUMA Injury
	pregnancy. Not outcomes	Infection, and Critical Care.
		2007. Vol 62 (4)
Pearlman, 1990	Not possible to assess full text	SR Méndez -Figueroa 2013
C-1:55 4007		
Schiff, 1997	Seat Bealt use. Protective factor of maternal	WJM, 1997. Vol. 167 (1)
Cohuston 2010	mortality after a MVC in Mexico	American lournal of Obstation
Schuster, 2016	Communication abstract. Impact of blunt	American Journal of Obstetric
	trauma on maternal and pregnancy outcome. MVC the most common injury mechanism	& Gynecology. Supplement to January 2016
	(70%). Pennsylvania Trauma Systems	
	Foundation Database (1996-2013).	
Schuster, 2018	Pennsylvania Trauma Systems Foundation	
JUNU3101, 2010	Database. ISS>9 and SBP<90mmHg are	, , , , , , , , , , , , , , , , , , ,
	predictors for poor outcomes after trauma	
	during pregnancy	
Sela, 2011	Treatment provided to pregnant motor	Annals of Surgery,
JC:0, 2011	vehicle accident (MVA) casualties in a mature	2011.Vol.254 (2)
	vehicle accident (MVA) casualties in a mature trauma system in Israel	2011.V0I.254 (2)

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Shah, 1998Trauma in general in pregnant womenJ Trauma. 1998 Jul;Shakerian 2015Determining adherence to recommended imaging guidelines in pregnant women from Victoria, AustraliaSR Petrone, 2017 J Trauma Acute Car. 2015.Vol. 78 (1)Shiff 2002Retrospective cohort study to assess outcomes of pregnant women hospitalized for injury in Washington State from 1989 to 1997SR Petrone, 2017 J Trauma. 2002; 53:Sirin, 2007Report the prevalence of seatbelt counselling by prenatal care providers during pregnancy in USAMatern Child Health 11:505–510Tinker 2010Risks factors involved in injuries in pregnant women from the National Birth Defects Prevention Study, USASR Petrone, 2017 Journal of Women's 2010. Vol. 19 (2)Van der Knoop, 2015Effect of maternal trauma in fetal motility at term and at one year of age trauma in pregnancySci Carly Human Devela (2015) 511–517Van der Knoop, 2018Matched case-control study. Neurobehavioral outcome in 6-18 year old children after trauma in pregnancyAccid Anal Prev. 20: Si33Vladutiu, 2013bSame sample Vladutiu 2013a; excluded as a secondary analysis from already included studySci Cail J. 2007.Wahabi, 200745 MVC case series pregnant women collected over a 10- year periodSR Petrone, 2017 Jury, Int. J. Care In 45 (2014) 1220-122Weiner 2016Minor trauma during pregnancy, not associated with adverse pregnancy outcomes, lsraelSR Petrone, 2017 Biry, Int. J. Care In 45 (2014) 1220-122Weiner 2016Minor trauma during pregnancy, not associated with adverse pregnancy outcomes, lsraelSR Petrone, 2017	
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frequent (45%)	ealth

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## maternal outcomes

2			
3 4	Study	ES (95% CI)	Trauma_severity
5	Placental abruption	I contraction of the second se	
6	Wolf, 1993	8.10 (5.02, 12.36)	NK
7	Miller, 2016	1.05 (0.29, 2.70)	NK
8	Schiff, 2005	130.95 (67.22, 222.24)	severe
9	Schiff, 2005		mild
10	Schiff, 2005	127.23 (95.92, 164.27)	mild-severe
11	Schiff, 2010	12.25 (8.80, 16.58)	mild
12	Vivian-Taylor, 2012	16.32 (11.26, 22.84)	mild-severe
13	Vladutiu, 2013a	7.17 (6.15, 8.31)	NK
14 15	Subtotal (I <sup>2</sup> = 96.7%, p = 0.00	15.41 (9.52, 21.30)	
15 16		10.11 (0.02, 21.00)	
16 17	Admission to hospital		
18	Vivian-Taylor, 2012	8.90 (5.28, 14.03)	mild-severe
19	Weiss, 2008	29.19 (21.94, 38.00)	NK
20	Subtotal (I <sup>2</sup> = .%, p = .)	13.33 (9.72, 16.95)	
20		13.33 (8.72, 10.33)	
21	Cesarean delivery		
23	Miller, 2016	6.06 (3.85, 9.08)	NK
24	Schiff, 2005	309.52 (213.14, 419.80)	
25	Schiff, 2005		
26	Schiff, 2005		
27	Schiff, 2003	<b>202.09</b> (219.27, 308.33) <b>259.26</b> (244.48, 274.46)	
28			
29	Vivian-Taylor, 2012		
30	Wolf, 1993		INK
31	Subtotal (I <sup>2</sup> = 99.7%, p = 0.00	215.33 (97.40, 333.26)	
32			
33	Labor induction		
34	Schiff, 2005		severe
35	Schiff, 2005		
36	Schiff, 2005		
37	Schiff, 2010		mild
38	Subtotal (I <sup>2</sup> = 87.0%, p = 0.00	228.25 (173.87, 282.63)	
39		The second s	
40	Maternal death	I contract of the second s	
41	Azar, 2005	6.57 (4.68, 8.97)	NK
42	Kvarnstrand, 2008	6.61 (3.70, 10.88)	mild-severe
43	Miller, 2016	0.26 (0.01, 1.47)	NK
44	Subtotal (I^2 = .%, p = .)	4.34 (-0.72, 9.41)	
45		The second s	
46	Premature Rupture of Membranes	The second s	
47	Schiff, 2005	11.90 (0.30, 64.55)	severe
48	Schiff, 2005	22.65 (9.16, 46.12)	mild
49	Schiff, 2005	20.36 (8.83, 39.71)	mild-severe
50	Vladutiu, 2013a 🛛 🗖	23.53 (21.66, 25.51)	NK
51	Whitehead, 2013	<b>95.72 (76.16, 118.34)</b>	NK
52	Subtotal (I^2 = 91.8%, p = 0.00	34.09 (13.89, 54.29)	
53			
54	Heterogeneity between groups: p = 0.000	The second s	
55	Overall (I^2 = 99.45%, p = 0.00;	<b>O</b> 75.74 (68.25, 83.24)	
56			
57			
58			
59	7023	420	
60	For	peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml	

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Schiff, 2010 Wolf, 193 Subtotal (M2 = .%, p = .) Feld distress Schiff, 2005 Schiff, 2005 Schif	Study			E	S (95% CI)	Trauma
Schiff 2010 Wolf, 1935 Subtotal (I*2 = 36, p = .) Felal disterss Schiff 2005 Schiff 2005 S	Fetal death					
Schiff, 2010 Wiler, 1903 Subtotal ( <sup>1/2</sup> = %, p = .) Fetal distress Subtotal ( <sup>1/2</sup> = %, p = .) Fetal distress Schiff, 2005 Schiff, 200	Kvarnstrand, 2008			11	.89 (7.85, 17.26)	mild-sev
Wolf, 1993       347 (159 a)         Subtolal (1°2 = .%, p = .)       5.88 (2.16, 9.79)         Fela distress       5.88 (2.16, 9.79)         Schiff, 2005       202.38 (122.54, 304.14)         Schiff, 2005       107.47 (65.73, 101.25)         Subtolal (1°2 = 93.6%, p = 0.00)       119.86 (67.96, 181.77)         Meconium at delivery       5.5hiff, 2005         Schiff, 2005       5.6 (2.42, 78.80)         Subtolal (1°2 = 0.9%, p = 0.90)       55.08 (2.16, 9.73)         Perinatal death       50.89 (31.36, 77.50)         Kvarnstrand, 2008       50.81 (2.20, 3.32)         Kvarnstrand, 2008       101.50 (67.96, 144.24)         Schiff, 2005       5.6hiff, 2005         Schiff, 2005       5.6hiff, 2005 </td <td></td> <td></td> <td></td> <td></td> <td>. ,</td> <td>mild</td>					. ,	mild
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Schiff, 2005 Schiff, 2010 Subtolal (M2 = 93.6%, p = 0.00) Meconium at delivery Schiff, 2005 Schiff, 2005 Schiff, 2005 Schiff, 2005 Subtolal (M2 = 0.0%, p = 0.99) Perinatal death Kvamstrand, 2008 Kvamstrand, 200	Schiff, 2005			• 20	2.38 (122.54, 304.14)	severe
Schiff, 2010       50.48 (43.31, 58.44)       r         Subtotal (№2 = 93.6%, p = 0.00)       119.86 (57.95, 181.77)         Meconium at delivery       50.52 (19.61, 133.47)         Schiff, 2015       46.54 (27.42, 78.80)         Subtotal (№2 = 0.0%, p = 0.99)       51.01 (44.30, 57.71)         Perinatal death       101.50 (67.96, 144.24)         Kvarnstrand, 2008       8.93 (4.77, 15.23)         Yvarnstrand, 2008       101.50 (67.96, 144.24)         Kvarnstrand, 2008       101.50 (67.96, 144.24)         Schiff, 2005       5.611 (2.05         Schiff, 2005       15.01 (45.6, 6.8)         Schiff, 2005       15.84 (16.7, 23.42)         Vidautiu, 2013a       5.25 (4.38, 6.23)         Subtotal (№2 = 92.3%, p = 0.00)       10.82 (19.6, 2.7)         Pretern delivery       5.55 (19.6, 58, 10.76)         Schiff, 2005       24.35 (19.8, 98.27.0)         Schiff, 2005       24.35 (19.8, 98.27.0)         Schiff, 2005       24.56 (198.6, 92.78)         Schiff, 2005       24.56 (198.6, 92.78)         Schiff, 2005       24.56 (198.6, 92.78)      <	Schiff, 2005		<b>—</b> —	11	9.74 (85.73, 161.25)	mild
Schiff, 2010       50.48 (43.31, 58.44)       r         Subtotal (№ 2 93.6%, p = 0.00)       119.86 (57.95, 181.77)         Meconium at delivery       55.52 (19.61, 133.47)         Schiff, 2005       48.54 (27.42, 78.80)         Schiff, 2005       51.01 (44.30, 57.71)         Perinatal death       101.50 (67.96, 144.24)         Kvarnstrand, 2008       8.93 (4.77, 15.23)         Kvarnstrand, 2008       77.15 (22.22.23)         Kvarnstrand, 2008       101.50 (67.96, 144.24)         Schiff, 2005       5.101 (44.30, 57.71)         Schiff, 2005       5.101 (44.30, 57.71)         Schiff, 2005       5.101 (52.31)         Schiff, 2005       15.18 (2.22, 23.9)         Yudautu, 2013a       5.25 (4.38, 6.23)         Subtotal (№2 = 92.3%, p = 0.00)       9         Preterm delivery       5.25 (4.38, 6.23)         Schiff, 2005       24.36 (198.96, 297.89)         Schiff, 2005       24.35 (198.69, 297.89)         Schiff, 2005       24.35 (198.69, 297.89)         Schiff, 2005       24.55 (198.61, 23.7)         Schiff, 2005       24.55 (198.69, 297.89)         Schiff, 2005       24.55 (198.69, 297.89)         Schiff, 2005       24.55 (198.69, 297.89)         Schiff, 2005       24.55 (198.6	Schiff, 2005			13	37.40 (104.94, 175.45)	mild-sev
Subtotal (h <sup>2</sup> = 93.6%, p = 0.00) Meconium at delivery Schiff, 2005 Schiff, 2005 Schiff, 2005 Subtotal (h <sup>2</sup> = 0.0%, p = 0.99) Perinatal death Kvarnstrand, 2008 Kvarnstrand, 2008 Miler, 2016 Schiff, 2005 Schiff, 2005 Schiff, 2005 Schiff, 2005 Schiff, 2005 Schiff, 2005 Schiff, 2005 Schiff, 2005 Subtotal (h <sup>2</sup> = 92.3%, p = 0.00) Preterm delivery Schiff, 2005 Schiff, 2005	Schiff, 2010				. ,	mild
Meconium at delivery       Schiff, 2005         Schiff, 2005       \$9.52 (19.61, 133.47)         Schiff, 2005       \$6.61, 2005         Schiff, 2010       \$0.68, 59.08)         Subtotal (1°2 = 0.0%, p = 0.99)       \$1.01 (44.30, 57.71)         Perinatal death       \$0.83, 47.7, 15.23)         Kvarnstrand, 2008       \$9.34, 47.7, 15.23)         Kvarnstrand, 2008       \$0.762, 22.22.92)         Kvarnstrand, 2008       \$0.762, 17.23, 30)         Kvarnstrand, 2008       \$0.790, 01.6, 2.31)         Miler, 2016       \$5.011, 32.66, 6.70)         Schiff, 2005       \$5.011, 20.05         Schiff, 2005       \$6.112, 22.33, 9, p = 0.00)         Pretern delivery       \$5.5117, 2005         Schiff, 2005       \$5.6117, 2005         Schiff, 2005       \$5.611, 13.347)         Schiff, 2005       \$2.66, 9, 6, 0, 0, 00)         Respiratory distress syndrome       \$2.56, 9, 16, 40.12, 9		: 0.00)				
Schiff. 2005       59.52 (19.61, 133.47)       5         Schiff. 2005       50.62 (19.61, 133.47)       5         Schiff. 2005       50.9 (31.62, 7.50)       50.8 (31.62, 7.50)         Schiff. 2005       50.9 (31.62, 7.50)       50.8 (31.62, 7.50)         Schiff. 2005       50.9 (31.62, 7.50)       50.0 (31.62, 7.50)         Schiff. 2005       50.10 (44.30, 57.71)       50.10 (44.30, 57.71)         Perinatal death       101.50 (67.96, 144.24)       s         Kvarnstrand, 2008       8.39 (4.77, 15.23)       r         Kvarnstrand, 2008       101.50 (67.92, 222.24)       s         Schiff. 2005       5.25 (4.38, 6.23)       10.8 (5.7, 37.6)         Schiff. 2005       5.25 (4.38, 6.23)       10.8 (6.27, 37.6)         Schiff. 2005       5.25 (4.38, 6.23)       10.8 (5.27, 37.6)         Schiff. 2005       1.78 (7.19, 36.35)       r         Schiff. 2005       5.25 (4.38, 6.23)       10.8 (6.52, 10.76)         Schiff. 2005       5.25 (4.38, 6.297.89)       10.9 (67.22, 222.24)       s         Schiff. 2005       5.30, p = 0.00)       8.06 (5.36, 10.76)       10.3 (10.6 4.3, 114.33)       10.3 (10.6 4.3, 114.33)         Viaon-Taylor, 2012       Viaon-Taylor, 2012       10.3 (10.6 4.3, 114.33)       10.3 (10.6 4.3, 114.33)       10.3 (10.6						
Schiff, 2005       48.54 (27.42, 78.80)       r         Schiff, 2010       50.98 (31.86, 59.08)       r         Subtotal (1°2 = 0.0%, p = 0.99)       51.01 (44.30, 57.71)         Perinatal death       101.50 (67.96, 144.24)       s         Kvamstrand, 2008       17.62 (12.62, 23.92)       r         Kvarnstrand, 2008       17.62 (12.62, 23.92)       r         Kvarnstrand, 2008       17.62 (12.62, 23.92)       r         Kvarnstrand, 2005       50.11 (3.66, 6.70)       N0.79 (0.16, 2.31)         Schiff, 2005       17.81 (7.19, 36.35)       r         Schiff, 2005       17.81 (7.19, 36.35)       r         Viadutiu, 2013       52.5 (4.38, 6.23)       s         Schiff, 2005       3.47 (15.9, 6.58)       s         Schiff, 2005       3.48 (2.9, 7.01)       r         Schiff, 2005       3.47 (15.9, 6.58)       s         Schiff, 2005       3.47 (15.9, 6.58)       s         Schiff, 2005       3.47 (15.9, 6.58)       s         Schiff, 2005       3.57 (40.00.44, 411.07)       s <t< td=""><td>-</td><td>1 I I I I I I I I I I I I I I I I I I I</td><td></td><td></td><td></td><td></td></t<>	-	1 I I I I I I I I I I I I I I I I I I I				
Schiff 2005 Schiff 2010 Subtotal (1/2 = 0.0%, p = 0.99) Perinatal death Kvamstrand, 2008 Kvamstrand, 2008 Kvamstrand, 2008 Kvamstrand, 2008 Kvamstrand, 2008 Schiff, 2005 Schiff, 2005 Schi			-			severe
Schiff, 2005 Schiff, 2010 Subtotal (1 <sup>1</sup> / <sup>2</sup> = 0.0%, p = 0.99) Perinatal death Kvamstrand, 2008 Kvamstrand, 2008 Kvamstrand, 2008 Kvamstrand, 2008 Kvamstrand, 2008 Schiff, 2005 Schiff, 200	Schiff, 2005			48	8.54 (27.42, 78.80)	mild
Schiff, 2010 Subtotal ( $h^2 = 0.0\%, p = 0.99$ ) Perinatal death Kvarnstrand, 2008 Kvarnstrand, 2008 Schiff, 2005 Schiff,						mild-sev
Subtotal ( $h^2 = 0.0\%, p = 0.99$ ) Perinatal death Kvarnstrand, 2008 Kvarnstrand, 2008 Kvarnstrand, 2008 Hyde, 2003 Miller, 2016 Schiff, 2005 Schiff,					. ,	mild
Perinatal death Kvarnstrand, 2008 Kvarnstrand, 2008 Hyde, 2003 Hyde, 2003 Hyde, 2003 Hyde, 2003 Schiff, 2005 Schiff, 2010 Wofr, 1993 Subtotal (h² = 82,4%, p = 0.00)		n 99) 👗				
Kvanstrand, 2008       101.50 (67.96, 144.24)       s         Kvanstrand, 2008       8.93 (4.77, 15.23)       r         Kvanstrand, 2008       5.01 (3.66, 6.70)       r         Hyde, 2003       0.79 (0.16, 2.31)       r         Schiff, 2005       23.81 (2.90, 83.37)       s         Schiff, 2005       17.76 (21.26, 22.39.2)       r         Vianta-Taylor, 2012       17.83 (35)       r         Vianta-Taylor, 2012       16.82 (11.87, 23.42)       r         Vialutiu, 2013a       5.25 (4.38, 6.23)       s         Schiff, 2005       3.47 (1.59, 6.58)       s         Schiff, 2005       3.66 (5.70, 20.11)       s         Schiff, 2005       3.66 (5.80, 10.76)       r         Schiff, 2005       3.66 (5.81, 10.76)       r         Schiff, 2005       9.66 (7.22, 22.22.4)       s         Schiff, 2005       9.67 (142, 95.80)       r         Schiff, 2005       9.7 (87.53, 107.92)       r         Schiff, 2005       9.6 (7.22, 222.24)       s         Schiff, 2005       9.7 (87.53, 107.92)       r         Schiff, 2005       9.7 (87.53, 107.92)       r         Schiff, 2005       9.7 (87.53, 107.92)       r         Schiff, 2005	(1 2 - 0.0 / 0, p - 0.0 / 0,	0.00)		51		
Kvarnstrand, 2008       8.93 (4.77, 15.23)       r         Kvarnstrand, 2008       17.62 (12.62, 23.92)       r         Hyde, 2003       0.13 (6, 6, 70)       r         Miller, 2016       23.81 (2.90, 83.37)       s         Schiff, 2005       23.81 (2.90, 83.37)       s         Schiff, 2005       16.18 (5.27, 37.60)       r         Yvian-Taylor, 2012       16.82 (11.67, 23.42)       r         Vladutiu, 2013a       5.25 (4.38, 6.23)       r         Subtotal (h*2 = 92.3%, p = 0.00)       4.16 (2.29, 7.01)       r         Preterm delivery       3.47 (1.59, 6.58)       8.06 (5.36, 10.76)         Schiff, 2005       245.95 (198.96, 297.89)       r         Schiff, 2005       245.95 (198.96, 297.89)       r         Schiff, 2005       3.47 (1.59, 6.58)       N         Subtotal (h*2 = 98.6%, p = 0.00)       *       97.37 (87.53, 107.92)       r         Viautui, 2013       *       *       93.09 (71.42, 95.98)       r         Whitehead, 2013       *       *       93.09 (71.42, 95.98)       r         Subtotal (h*2 = 98.6%, p = 0.00)       *       *       93.05 (15.88, 52.73)       r         Schiff, 2010       *       *       93.05 (15.88, 52.73)       r						
Kvarnstrand, 2008       8.93 (4.77, 15.23)       r         Kvarnstrand, 2008       17.62 (12.62, 23.92)       r         Hyde, 2003       0.78 (0.16, 2.31)       5.01 (3.66, 6.70)         Miller, 2016       23.81 (2.90, 83.37)       s         Schiff, 2005       23.81 (2.90, 83.37)       s         Schiff, 2005       16.18 (5.27, 37.36)       r         Vian-Taylor, 2012       16.82 (11.67, 23.42)       r         Viadutiu, 2013a       5.25 (4.38, 6.23)       r         Schiff, 2005       3.47 (1.59, 6.58)       s         Subtotal (h² = 92.3%, p = 0.00)       3.47 (1.59, 6.58)       s         Preterm delivery       3.47 (1.59, 6.58)       s         Schiff, 2005       245.95 (198.96, 297.89)       r         Schiff, 2005       245.95 (198.96, 297.89)       r         Schiff, 2010       **       9.3 (47 (1.59, 6.58)       s         Viautuiu, 2013a       **       10.33 (106.43, 114.33)       r         Schiff, 2005       **       9.3 (47 (1.49, 59.80)       r         Schiff, 2005       **       9.52 (19.61, 133.47)       s         Schiff, 2005       **       **       9.52 (19.61, 133.47)       s         Schiff, 2005       5.9, 52 (19.61, 133.47)	Kvarnstrand, 2008			10	1.50 (67.96, 144.24)	severe
Kvanstrand, 2008       17.62 (12.62, 23.92)         Hyde, 2003       5.01 (3.66, 6.70)         Miller, 2016       0.79 (0.16, 2.31)         Schiff, 2005       16.18 (5.27, 37.36)         Schiff, 2005       17.81 (7.19, 36.35)         Viaun-Taylor, 2012       16.82 (11.67, 23.42)         Vladutiu, 2013a       5.25 (4.38, 6.23)         Schiff, 2005       5.26 (4.38, 6.23)         Schiff, 2010       4.18 (2.29, 7.01)         Wolf, 1993       3.47 (1.59, 6.58)         Subtotal (h² = 92.3%, p = 0.00)       9         Preterm delivery       Schiff, 2005         Schiff, 2005       97.37 (87.53, 107.92)         Yolautiu, 2013a       97.37 (87.53, 107.92)         Yolautiu, 2013a       97.37 (87.53, 107.92)         Schiff, 2005       97.37 (87.53, 107.92)         Schiff, 2005       97.37 (87.53, 107.92)         Subtotal (h² = 98.6%, p = 0.00)       97.37 (87.53, 107.92)         Respiratory distress syndrome Schiff, 2005       96.59, 19.86, 52.73)         Schiff, 2005       30.53 (15.88, 52.73)         Schiff, 2005       30.53 (15.88, 52.73)         Schiff, 2010       14.64 (10.85, 19.30)         Wolf, 1993       8.61 (7.24, 25.19)         Subtotal (h² = 82.4%, p = 0.00)       16.56 (7.94, 25.						mild
Hyde, 2003       5.01 (3.66, 6.70)       N         Miller, 2016       0.79 (0.16, 2.31)       2.38 (1 2.90, 83.37)       s         Schiff, 2005       16.18 (5.27, 37.36)       17.81 (7.19, 36.35)       17.81 (7.19, 36.35)         Viautria, 2013       5.25 (4.38, 6.23)       16.82 (2.90, 73.342)       16.82 (2.90, 73.342)         Viautria, 2013       5.25 (4.38, 6.23)       17.81 (7.19, 36.35)       17.81 (7.19, 36.35)         Subtotal (l*2 = 92.3%, p = 0.00)       4.18 (2.29, 7.01)       16.82 (1.67, 23.42)       18.06 (5.36, 10.76)         Preterm delivery       Schiff, 2005       8.06 (5.36, 10.76)       130.95 (67.22, 222.24)       s         Schiff, 2005       Schiff, 2005       9.00)       9.00       9.00       130.95 (67.22, 222.24)       s         Schiff, 2005       Schiff, 2005       9.00       9.00       9.00       130.95 (67.22, 222.24)       s         Schiff, 2005       Schiff, 2010       9.00       9.00       9.00       9.00       9.00       9.00       10.30 (106.43, 114.33)       10.33 (106.43, 114.33)       10.33 (106.43, 114.33)       10.33 (106.43, 114.33)       10.33 (106.43, 114.33)       10.33 (106.43, 114.33)       10.33 (106.43, 114.33)       10.33 (106.44, 110, 7.07)       187.07 (141.39, 232.74)       187.07 (141.39, 232.74)       187.07 (141.39, 232.74)       187.07 (1						mild-sev
Miller, 2016       0.79 (0.16, 2.31)         Schiff, 2005       23.81 (2.90, 83.37)         Schiff, 2005       16.18 (5.27, 37.36)         Schiff, 2012       16.22, 17.36)         Vladutu, 2013a       52.54 (4.38, 6.23)         Subtotal (h² = 92.3%, p = 0.00)       8.06 (5.36, 10.76)         Preterm delivery       3.47 (1.59, 6.58)         Schiff, 2005       130.95 (67.22, 222.24)         Schiff, 2005       10.33 (106.43, 114.33)         Schiff, 2005       110.33 (106.43, 114.33)         Schiff, 2005       110.33 (106.43, 114.33)         Schiff, 2005       130.51 (14.139, 232.74)         Schiff, 2005       14.64 (10.85, 19.30)						NK
Schiff, 2005       23.81 (2.90, 83.37)       s         Schiff, 2005       16.18 (5.27, 37.36)       17.81 (7.19, 36.35)       r         Vivian-Taylor, 2012       16.82 (11.67, 23.42)       r       16.82 (11.67, 23.42)       r         Vidutiu, 2013a       5.25 (4.38, 6.23)       8.06 (5.36, 10.76)       8.06 (5.36, 10.76)       8.06 (5.36, 10.76)         Preterm delivery       Schiff, 2005       8.06 (5.36, 10.76)       8.06 (5.36, 10.76)       97.37 (87.53, 107.92)       r         Schiff, 2005       Schiff, 2005       8.06 (5.36, 10.76)       97.37 (87.53, 107.92)       r       97.37 (87.53, 107.92)       r         Viaun-Taylor, 2012       •       •       8.09 (71.42, 95.98)       r       221.377 (400.94, 471.07)       r         Viadutiu, 2013a       Whitehead, 2013       •       •       8.09 (71.42, 95.98)       r       4.35.77 (40.04, 471.07)       r         Schiff, 2005       59.52 (19.61, 133.47)       s       59.52 (19.61, 133.47)       s       22.65 (9.16, 46.12)       r         Schiff, 2005       59.52 (19.61, 133.47)       s       59.52 (19.61, 133.47)       s       22.65 (9.16, 46.12)       r         Schiff, 2005       59.52 (19.61, 133.47)       s       59.52 (19.61, 133.47)       s       22.65 (9.16, 46.12)       r <t< td=""><td>•</td><td><b>F</b> 1</td><td></td><td></td><td></td><td>NK</td></t<>	•	<b>F</b> 1				NK
Schiff, 2005       16.18 (5.27, 37.36)         Schiff, 2005       17.81 (7.19, 36.35)         Vivian-Taylor, 2012       16.82 (11.67, 23.42)         Vidautiu, 2013a       5.25 (4.38, 6.23)         Schiff, 2010       4.18 (2.29, 7.01)         Wolf, 1993       3.47 (1.59, 6.58)         Subtotal (1^2 = 92.3%, p = 0.00)       9         Preterm delivery       3.47 (1.59, 6.58)         Schiff, 2005       13.95 (67.22, 222.24)         Schiff, 2005       245.95 (198.96, 297.89)         Schiff, 2005       245.95 (198.96, 297.89)         Schiff, 2005       97.37 (87.53, 107.92)         Vivian-Taylor, 2012       9         Vidautiu, 2013a       97.37 (87.53, 107.92)         Whitehead, 2013       90 (71.42, 95.98)         Subtotal (1^2 = 98.6%, p = 0.00)       9         Respiratory distress syndrome       59.52 (19.61, 133.47)         Schiff, 2005       22.65 (9.16, 46.12)         Schiff, 2005       93.53 (15.88, 52.73)         Schiff, 2005       14.64 (10.85, 19.30)         Schiff, 2						
Schiff, 2005 Vivian-Taylor, 2012 Vladutiu, 2013a Schiff, 2010 Wolf, 1993 Subtotal (I^2 = 92.3%, p = 0.00) Preterm delivery Schiff, 2005 Schiff, 2005 Schiff, 2010 Vivian-Taylor, 2012 Vladutiu, 2013a Whitehead, 2013 Subtotal (I^2 = 98.6%, p = 0.00) Respiratory distress syndrome Schiff, 2005 Schiff, 2005 Schi						severe
Vivian-Taylor, 2012       16.82 (11.67, 23.42)         Vladutiu, 2013a       5.25 (4.38, 6.23)         Schiff, 2010       4.18 (2.29, 7.01)         Wolf, 1993       3.47 (15.9, 6.58)         Subtotal (I^2 = 92.3%, p = 0.00)       8.06 (5.36, 10.76)         Preterm delivery       3.09 (67.22, 222.24)         Schiff, 2005       245.95 (198.96, 297.89)         Schiff, 2005       245.95 (198.96, 297.89)         Schiff, 2010       97.37 (87.53, 107.92)         Viautiu, 2013a       110.33 (106.43, 114.33)         Whitehead, 2013       3.09 (71.42, 95.98)         Subtotal (I^2 = 98.6%, p = 0.00)       435.77 (400.94, 471.07)         Respiratory distress syndrome       50.52 (19.61, 133.47)         Schiff, 2005       30.53 (15.88, 52.73)         Schiff, 2005       30.53 (15.88, 52.73)         Schiff, 2005       14.64 (10.85, 19.30)         Schiff, 2010       4.64 (10.85, 19.30)         Wolf, 1993       50.51 (15.88, 52.73)         Subtotal (I^2 = 82.4%, p = 0.00)       16.56 (7.94, 25.19)						mild
Vladutiu, 2013a       5.25 (4.38, 6.23)         Schiff, 2010       4.18 (2.29, 7.01)         Wolf, 1993       3.47 (1.59, 6.58)         Subtotal (l^2 = 92.3%, p = 0.00)       8.06 (5.36, 10.76)         Preterm delivery       130.95 (67.22, 222.24)         Schiff, 2005       245.95 (198.96, 297.89)         Schiff, 2005       221.37 (181.29, 265.71)         Schiff, 2010       97.37 (87.53, 107.92)         Viautiu, 2013a       Whitehead, 2013         Whitehead, 2013       110.33 (106.43, 114.33)         Subtotal (l^2 = 98.6%, p = 0.00)       187.07 (141.39, 232.74)         Respiratory distress syndrome       59.52 (19.61, 133.47)         Schiff, 2005       22.65 (9.16, 46.12)         Schiff, 2005       30.53 (15.88, 52.73)         Schiff, 2005       22.65 (9.16, 46.12)         Schiff, 2005       14.64 (10.85, 19.30)         Schiff, 2010       14.64 (10.85, 19.30)         Wolf, 1993       6.17 (3.53, 10.00)         Subtotal (l^2 = 82.4%, p = 0.00)       16.56 (7.94, 25.19)					. ,	mild-sev
Schiff, 2010       4.18 (2.29, 7.01)         Wolf, 1993       3.47 (1.59, 6.58)         Subtotal (I^2 = 92.3%, p = 0.00)       8.06 (5.36, 10.76)         Preterm delivery       8.06 (5.36, 10.76)         Schiff, 2005       245.95 (198.96, 297.89)         Schiff, 2010       97.37 (87.53, 107.92)         Vivian-Taylor, 2012       97.37 (87.53, 107.92)         Vladutiu, 2013a       97.37 (87.53, 107.92)         Subtotal (I^2 = 98.6%, p = 0.00)       97.37 (40.94, 471.07)         Respiratory distress syndrome       95.52 (19.61, 133.47)         Schiff, 2005       22.65 (9.16, 46.12)         Schiff, 2005       30.53 (15.88, 52.73)         Schiff, 2005       30.53 (15.8		<b>.</b> :				mild-sev
Wolf, 1993       3.47 (1.59, 6.58)       N         Subtotal (I^2 = 92.3%, p = 0.00)       8.06 (5.36, 10.76)       130.95 (67.22, 222.24)       s         Preterm delivery       Schiff, 2005       245.95 (198.96, 297.89)       130.95 (67.22, 222.24)       s         Schiff, 2005       Schiff, 2010       97.37 (87.53, 107.92)       130.95 (67.22, 222.24)       s         Vivian-Taylor, 2012       Vidautiu, 2013a       97.37 (87.53, 107.92)       110.33 (106.43, 114.33)       N         Whitehead, 2013       Subtotal (I^2 = 98.6%, p = 0.00)       9.52 (19.61, 133.47)       s       22.65 (9.16, 46.12)       187.07 (141.39, 232.74)         Respiratory distress syndrome       Schiff, 2005       30.53 (15.88, 52.73)       14.64 (10.85, 19.30)       14.64 (10.85, 19.30)       16.56 (7.94, 25.19)         Wolf, 1993       Subtotal (I^2 = 82.4%, p = 0.00)       Image: Construction of the second of the				5.	25 (4.38, 6.23)	NK
Wolf, 1993       3.47 (1.59, 6.58)       N         Subtotal (I^2 = 92.3%, p = 0.00)       8.06 (5.36, 10.76)       130.95 (67.22, 222.24)       s         Preterm delivery       Schiff, 2005       245.95 (198.96, 297.89)       n       221.37 (181.29, 265.71)       n         Schiff, 2010       Vivian-Taylor, 2012       Vladutiu, 2013a       97.37 (87.53, 107.92)       n       110.33 (106.43, 114.33)       N         Whitehead, 2013       Subtotal (I^2 = 98.6%, p = 0.00)       83.09 (71.42, 95.98)       n       110.33 (106.43, 114.33)       N         Respiratory distress syndrome       59.52 (19.61, 133.47)       s       22.65 (9.16, 46.12)       n         Schiff, 2005       Schiff, 2005       30.53 (15.88, 52.73)       n       14.64 (10.85, 19.30)       n         Subtotal (I^2 = 82.4%, p = 0.00)       Image: State of the state of	Schiff, 2010			4.	18 (2.29, 7.01)	mild
Subtotal (I^2 = 92.3%, p = 0.00)       8.06 (5.36, 10.76)         Preterm delivery       30.95 (67.22, 222.24)       se         Schiff, 2005       245.95 (198.96, 297.89)       221.37 (181.29, 265.71)         Schiff, 2010       97.37 (87.53, 107.92)       97.37 (87.53, 107.92)         Vivian-Taylor, 2012       Vladutiu, 2013a       91.06 (43, 114.33)         Whitehead, 2013       91.000       83.09 (71.42, 95.98)       110.33 (106.43, 114.33)         Subtotal (I^2 = 98.6%, p = 0.00)       95.52 (19.61, 133.47)       82.265 (9.16, 46.12)       187.07 (141.39, 232.74)         Respiratory distress syndrome       59.52 (19.61, 133.47)       82.265 (9.16, 46.12)       14.64 (10.85, 19.30)       14.64 (10.85, 19.30)         Schiff, 2005       30.53 (15.88, 52.73)       14.64 (10.85, 19.30)       16.56 (7.94, 25.19)						NK
Preterm delivery       130.95 (67.22, 222.24)       s         Schiff, 2005       Schiff, 2005       245.95 (198.96, 297.89)       p         Schiff, 2010       Vivian-Taylor, 2012       Yladutiu, 2013a       97.37 (87.53, 107.92)       p         Vladutiu, 2013a       Whitehead, 2013       110.33 (106.43, 114.33)       M         Schiff, 2005       Schiff, 2005       130.95 (67.22, 222.24)       s         Schiff, 2010 $\bullet$ 97.37 (87.53, 107.92)       p         Vladutiu, 2013a       Whitehead, 2013       110.33 (106.43, 114.33)       M         Subtotal (h <sup>2</sup> 2 = 98.6%, p = 0.00) $\bullet$ 187.07 (141.39, 232.74)       187.07 (141.39, 232.74)         Respiratory distress syndrome       Schiff, 2005       Schiff, 2005       Schiff, 2005       Schiff, 2005       Schiff, 2005       Schiff, 2005       Schiff, 2010       14.64 (10.85, 19.30)       m         Wolf, 1993       Subtotal (h <sup>2</sup> 2 = 82.4%, p = 0.00) $\bullet$ 16.56 (7.94, 25.19)       16.56 (7.94, 25.19)		: 0.00)				
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Respiratory distress syndrome       59.52 (19.61, 133.47)       s         Schiff, 2005       22.65 (9.16, 46.12)       n         Schiff, 2005       30.53 (15.88, 52.73)       n         Schiff, 2010       14.64 (10.85, 19.30)       n         Wolf, 1993       6.17 (3.53, 10.00)       N         Subtotal ( $l^2 = 82.4\%$ , $p = 0.00$ ) $\blacklozenge$ 16.56 (7.94, 25.19)		0.00			. ,	INIX
Schiff, 2005       59.52 (19.61, 133.47)       s         Schiff, 2005       22.65 (9.16, 46.12)       m         Schiff, 2010       30.53 (15.88, 52.73)       m         Wolf, 1993       6.17 (3.53, 10.00)       M         Subtotal (l^2 = 82.4%, p = 0.00)       16.56 (7.94, 25.19)       16.56 (7.94, 25.19)	Subtotal (1/2 = 98.6%, p =	0.00)		18	37.07 (141.39, 232.74)	
Schiff, 2005       59.52 (19.61, 133.47)       s         Schiff, 2005       22.65 (9.16, 46.12)       m         Schiff, 2010       30.53 (15.88, 52.73)       m         Wolf, 1993       6.17 (3.53, 10.00)       M         Subtotal (l^2 = 82.4%, p = 0.00)       16.56 (7.94, 25.19)       16.56 (7.94, 25.19)	Respiratory distress syndr	ome				
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Outcome	Total sample size	Incidence estimate per 1,000 women (95%CI)
Maternal outcomes		
Placental problems	235329	100.00 (98.79, 101.22)
Miscarriage	3794	1.85 (0.74, 3.80)
Antepartum haemorrhage	2022	47.48 (38.62, 57.67)
Postpartum haemorrhage	2022	77.65 (66.35, 90.18)
Vaginal bleeding	235329	247.00 (245.26, 248.75)
Hospital stay >=6 days	5936	117.92 (109.82, 126.40)
Maternal death or hospitalisation	32810	135.05 (131.37, 138.80)
Fetal and neonatal		
Hypoxia	582	22.34 (11.95, 37.89)
Neonatal death	2270	5.73 (3.05, 9.77)
Neonatal transfer	2022	42.53 (34.16, 52.26

Appendix 5. Incidence of maternal, fetal & neonatal complications from single studies

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Outcome	Study ID	Number of events	Group size	Trauma severity level
Admission to hospital	Brookfield, 2013	182	256	Not given
	Chibber, 2015	648	728	Not given
Caesarean delivery	Chibber, 2015	529	728	Not given
	Luley 2013	32	126	Not given
	Orji, 2002	2	84	Not given
Fetal death	Aboutanos, 2007	1	148	Not given
	Chibber, 2015	78	728	Not given
Fetal distress	Chibber, 2015	412	728	Not given
Fetal tachycardia	Orji, 2002	10	84	Not given
Hydrops fetalis	Aboutanos, 2007	1	148	Not given
Maternal death	Aboutanos, 2007	0	148	Not given
	Baerga-Varela, 2000	1	39	Severe
	Brookfield, 2013	7	256	Not given
	Chibber, 2015	100	728	Not given
Maternal death	Orji, 2002	2	84	Not given
Miscarriage	Aboutanos, 2007	5	148	Not given
	Baerga-Varela, 2000	7	39	Mild to severe
Perinatal death	Baerga-Varela, 2000	23	39	Mild to severe
	Luley 2013	6	126	Not given
	Orji, 2002	3	84	Not given
Placental abruption	Chibber, 2015	428	728	Not given
	Luley 2013	7	126	Not given
	Orji, 2002	1	84	Not given
Preterm delivery	Chibber, 2015	97	728	Not given
Uterine rupture	Chibber, 2015	12	728	Not given
	Orji, 2002	1	84	Not given

## PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported or page #
TITLE		·	
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1
ABSTRACT	·	·	
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	2-3
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	4
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	5
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	5
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	5-7
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	5
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	Appendix 1
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	5-6, Appendix 2
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	6-7
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	5-7
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	7
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	7-8
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g. geel <sup>2</sup> ) for each meta analysis com/site/about/guidelines.xhtml	8

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# PRISMA 2009 Checklist

Page	1	of	2
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Page 1 of 2			
Section/topic	#	Checklist item	Reported on page #
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	7-8
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	7-8
4 Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	8, Figure 1
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	8, Table 1
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	8, 9, Figure 2
2 Results of individual studies 3 4 5 6 7 8	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	9,10 Table 2, Figure 3 Figure S1,S2 Appendix 5, 6
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	10, Appendix 3, 4
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	8,9 Figure 2
5 6 Additional analysis 7 8	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	9,10 Figure S1, S2
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	10
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias). For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml	11
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4 5	Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	12
6	FUNDING			
7 8 9	Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	3
9 10	From: Moher D, Liberati A, Tetzlaff , doi:10.1371/journal.pmed1000097	J, Altm	an DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med I For more information, visit: www.prisma-statement.org. Page 2 of 2	6(7): e1000097.
42 43 44 45 46 47			For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml	

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#### Maternal trauma due to motor vehicle crashes and pregnancy outcomes: A systematic review and metaanalysis

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Manuscript ID	bmjopen-2019-035562.R2
Article Type:	Original research
Date Submitted by the Author:	09-Jul-2020
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<b>Primary Subject Heading</b> :	Public health
Secondary Subject Heading:	Obstetrics and gynaecology, Medical publishing and peer review
Keywords:	ACCIDENT & EMERGENCY MEDICINE, EPIDEMIOLOGY, OBSTETRICS

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3 4	1	Maternal trauma due to motor vehicle crashes and pregnancy outcomes: A systematic review
4 5	2	and meta-analysis
6 7	3	
8	4	Amezcua-Prieto C <sup>1,2,3</sup> , Ross J <sup>4</sup> , Rogozińska E, <sup>5,6</sup> Mighiu P <sup>5</sup> , Martínez-Ruiz V <sup>1,2,3</sup> , Brohi K <sup>4</sup> , Bueno-
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59 60	55

# Objectives To systematically review and quantify the effect of motor vehicle crashes (MVC) in pregnancy on maternal and offspring outcomes.

32 Design

Abstract

33 Systematic review and meta-analysis of observational data searched from inception until July 1, 2018.

34 Searching was from June to August 2018 in Medline, Embase, Web of Science, Scopus, LILACS

35 SciELO, TRANSPORT, IRRD, TRANSDOC, CDSR, and Cochrane Central Register CENTRAL.

36 Participants

Studies were selected if they focused on the effects of exposure MVC during pregnancy vs. nonexposure, with follow up to verify outcomes in various settings, including secondary care, collision and
emergency, and inpatient care.

#### 40 Data synthesis

For incidence data, we calculated a pooled estimate per 1,000 women. For comparison of outcomes
between women involved and those not involved in MVC, we calculated odds ratios with 95%
confidence intervals. Where possible, we statistically pooled the data using the random-effects model.
The quality of studies used in the comparative analysis was assessed with Newcastle-Ottawa Scale.

45 **Results** 

We included 19 studies (3,222,066 women) of which the majority was carried out in high-income 6 7 countries (18/19). In population-level studies of women involved in MVC, maternal death occurred in 8 3.6 per 1,000 (95% CI 0.25 to 10.42; 3 studies, 12,000 women; Tau= 1.77), and fetal death or stillbirth 9 in 6.6 per 1,000 (95% CI 3.81 to 10.12; 8 studies, 47,992 women; I<sup>2</sup>=92.6%). Pooled incidence of 0 complications per 1,000 women involved in MVC was labour induction (276.43), preterm delivery 1 (191.90) and caesarean section (166.65). Compared to women not involved in MVC, those involved had increased odds of placental abruption (OR 1.43, 95% CI 1.27 to 1.63; 3 studies, 1,500,825 women) 2 and maternal death (OR 202.27; 95% CI 110.60 to 369.95; 1 study, 1,094,559 women). 3

54 Conclusion: Pregnant women involved in MVC were at higher risk of maternal death and55 complications than those not involved.

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56	PROSPERO registration: CRD42018100788										
57	Key terms: Pregnancy; motor vehicle crashes; pregnancy complications										
58	Word count: 300										
59	Strengths and limitations of this study										
60	• This is the first systematic review examining the link between involvement in MVC,										
61	mortality and adverse outcomes that includes evaluation of study quality assessment.										
62	• This is the second systematic review looking at outcomes following MVC in pregnancy.										
63	• We conducted our review using a prospectively registered protocol and reported it in										
64	accordance with the international standards.										
65	• Outcomes variables correspond to any trimester, not to specific trimesters.										
66	• Outcomes according to seatbelt use are scarce, since only two studies use population-level										
67	data.										
68	Funding statement										
69	This research received no specific grant from any funding agency in the public, commercial or not-										
70	for-profit sectors.										
71	Competing interest's statement										
72	There are non-financial associations that may be relevant to the submitted manuscript.										
73											

#### 74 Introduction

Up to half of all women in developed countries drive motor vehicles (1) and the consequences of road traffic-related injuries involving pregnant women can be severe (2). Indeed, motor vehicle crashes (MVC) are the most common cause of non-obstetric trauma associated with fetal deaths (2.3 per 100,000 live births) (3). The risk of adverse outcomes resulting from an MVC increases in the second trimester of pregnancy if the pregnant women were the driver (4); however, this does not appear to be the case for pregnant passengers or pedestrians (5). A maternal mortality rate of 3.5 women per 100,000 is reported following MVCs in pregnant women (6). Mechanisms of injury recorded within the pregnant population of the UK national trauma registry, the Trauma Audit and Research Network (TARN), saw an increased rate of vehicular collision in pregnant women when compared to the non-pregnant cohort (7). In 2001-2008, 2.9% of pregnant women in North Carolina were drivers in one or more crashes (8). In the USA, data from the National Automotive Sampling System (NASS/CDS) reflects that when vehicles with pregnant women are involved in collision, 50% of those women will sustain an injury(9). There are few safety guidelines on travelling by car during pregnancy (10-12). The focus of these tends to be on questions around the use of seatbelts and the activation of airbags in the car (12).

There is a reported association between MVC and maternal mortality (13). Moreover, further associations such as the trigger for immediate delivery or being more likely to die are reported with severe blunt injury (Injury Severity Score (ISS) of 9 or above, or systolic blood pressure (SBP) <90mmHg on arrival) (14). Involvement in MVC is also associated with perinatal mortality (15), injuries to the abdominal region (16), placental abruption secondary to increased intra-abdominal pressure (17), preterm birth, and caesarean section (6). However, more data are required in relation to areas such as fetal outcomes and higher risk pregnancies, particularly regarding sociodemographic characteristics of the mother, specific trimester of pregnancy when exposed to trauma, socioeconomic country conditions, severity and type of trauma, and collision characteristics such as speed. A systematic review on trauma in pregnancy (including five studies reporting complications of involvement in MVC, and fourteen other studies on others form of trauma) showed that MVC and

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domestic violence were the most common causes of traumatic injury during pregnancy (4). No quality assessment of the included studies was reported in this review. Previous non-systematic reviews have published strategies used to monitor women and fetuses after a crash (18-21). However, to our knowledge there is no systematic review or meta-analysis focused on the maternal and fetal outcomes after MVC in pregnancy. **Review** objectives As the clinical impact on the mother and fetus after MVC has not been well documented, we conducted a systematic review of the effect on maternal and fetal outcomes of MVC in pregnant women, compared to those not involved in a collision. **Methods** We conducted a systematic review and reported it according to recommended standards (22). The review was prospectively registered with PROSPERO (no. CRD42018100788). *Literature search* Searching was from June to August 2018. The following databases were used to identify relevant literature: Medline, Embase, Web of Science, Scopus, LILACS (Latin-American and Caribbean System on Health Sciences Information), Science Citation Index, SciELO (Scientific Electronic Library Online), TRANSPORT, IRRD (International Road Research Documentation), TRANSDOC (European Conference of Ministers of Transportation databases), Cochrane Database of Systematic Reviews (CDSR), and Cochrane Central Register of Controlled Trials (CENTRAL). We also sought to identify unpublished research or research reported in the grey literature by searching a range of relevant databases, including the Inside Conferences, Systems for Information on Grey Literature (SIGLE) and Dissertation Abstracts. Furthermore, the searches of the medical database were supplemented with the Internet search using a general search engine (e.g. Google, www.google.co.uk/) and safetylit.org. Language and date restrictions were not applied to electronic searches. Relevant studies were identified using a combination of, but not limited to, the medical subject headings (MeSH) and keywords for 

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"motor vehicle collision" (OR road traffic collision OR crash OR collision) and "pregnancy" (OR

pregnant women OR gravid women OR childbearing women OR maternal).

7 8	132	
9 10	133	Review inclusion criteria
11 12	134	Papers were selected if they studied the effects of exposure to trauma due to involvement in an MVC
13 14	135	during pregnancy vs. non-exposure, with follow up to verify outcomes in various settings including
15 16	136	secondary care, collision and emergency, and inpatient care. Observational studies (cohort studies, case-
17 18 19	137	control design, non-intervention arms of randomised controlled trials) were included. Case series and
20 21	138	case reports were excluded. Appendix 1 shows the search strategy for Medline (via Ovid) and Appendix
22 23	139	2 the excluded studies with reasons.
24 25	140	
26 27	141	Data extraction and study quality assessment
28 29	142	A double screening of papers was carried out. Two reviewers (CAP & JR) independently extracted the
30 31	143	relevant data from each full-text article and data were recorded using a standardized data extraction
32 33	144	form. A data extraction form was piloted for each study design and amended as required. Discrepancies
34 35 26	145	were resolved by consensus or by a discussion with a third senior author (ER). We extracted data on a)
36 37 38	146	severe adverse maternal outcomes such as maternal death, miscarriage and preterm birth (<37/40 and
39 40	147	<34/40); b) severe adverse fetal outcomes such as intrauterine death/stillbirth and neonatal death.
41 42	148	Secondary outcomes were: a) individual components of maternal outcomes such as preterm labour,
43 44	149	mode of delivery (vaginal delivery vs caesarean section), premature rupture of membranes (PROM),
45 46	150	preterm premature rupture of membranes (PPROM), placental abruption, chorioamnionitis/sepsis and
47 48	151	maternal admission to an intensive care unit (ICU) or high dependency unit (HDU); b) individual
49 50	152	components of fetal outcomes: respiratory distress syndrome, neonatal ICU admission, low birth weight
51 52	153	(LBW) and small for gestational age (SGA).
53 54	154	
55 56 57	155	We also extracted data on 1) adverse outcomes in pregnant women involved in MVC and their offspring
57 58 59	156	in subgroups according to maternal characteristics (low, high and any risk), trimester of exposure,
60	157	country (low and middle income, high income), type of trauma (penetrating, blunt, burns), severity of
		6

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trauma (mild, moderate, severe), seatbelt use (yes, no), study quality (low, high); 2) risk factors for pregnancy complications following MVC such as maternal characteristics (age, parity, high risk pregnancy, gestational age), type of trauma, type of motor vehicle, type of collision, collision characteristic (stationary, high or moderate speed) and seat belt use.

The quality assessment of studies was independently evaluated by two reviewers (JR and CAP) using the Newcastle-Ottawa Scale (23). This scale includes 8 items, 4 items about selection criteria of cases or cohorts in case-control or cohort designs, respectively; 2 items about comparability between groups (in both designs); and 3 items about exposure criteria in case-control designs and about outcomes in cohort designs. Any of those studies could be awarded a maximum of one star for each numbered item within the selection and exposure categories. A maximum of two stars could be given for comparability. For the incidence analysis, we considered six aspects (24): 1) representativeness of cohort; 2) design; 3) method of sampling; 4) adequacy of follow-up; 5) if the outcomes were adequately ascertained and 4) if measurement or misclassification bias were minimized. Studies without these features or with unclear reporting were classified to have a high risk of bias. 

Patient and Public Involvement 

"No patient involved"

Data synthesis

We undertook random-effects meta-analysis to determine the odds ratios (OR) with 95% confidence intervals (CI) for maternal and offspring complications from MVC. We estimated heterogeneity between the included studies with Chi-Square test of Q (I2) excepting when not enough studies were in the meta-analysis (2-3), and we pooled the rates of maternal/fetal complications and reported with 95% CI. For each primary outcome, a meta-analysis was conducted for studies sufficiently homogeneous in terms of the characteristics of participants and exposure. The subgroup analysis was applied in: a) trimester of pregnancy during which the trauma occurred; b) maternal risk status (low, high, any risk); c) type of trauma; d) severity of trauma (using the ISS to categorize the severity of trauma sustained following MVC) (25); e) setting (low and middle income, high-income country); f) year of study

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3 4	185	publication: (before or after the introduction of mandatory seatbelt legislature in the country of study);
5 6	186	and g) study quality according to the Newcastle and Ottawa Scale (23).
7 8	187	
9 10	188	Results
11 12 12	189	Study selection
13 14 15	190	Out of 1,739 retrieved references, 19 studies met the eligibility criteria (Figure 1). Five of these reported
16 17	191	data allowing us to compare pregnancy complications between pregnant women involved in MVC and
18 19	192	those not involved in MVC (6, 26-29). The totality of the studies $(n = 19)$ contributed to the analysis of
20 21	193	the incidence of pregnancy complications among women involved in MVC (6, 17, 26-42).
22 23	194	
24 25	195	Characteristics of included studies
26 27	196	The characteristics of included studies are in Table 1. Included studies were published between 1993
28 29	197	and 2016. Most of them were carried out in developed, high-income countries such as USA (14/18) (26,
30 31	198	28-31, 33-41), Sweden (1/19) (27), Kuwait (1/19) (17) and Israel (1/19) (42). The number of included
32 33 34	199	pregnant women varies, ranging from 39 to 1,094,559. The data was sourced from hospital
35 36	200	records/trauma registries (7/19) (17, 31, 32, 35, 38, 39, 42) or from population-level databases (12/19)
37 38	201	(6, 26-30, 33, 34, 36, 37, 40, 41). The majority of studies collected information on outcomes of pregnant
39 40	202	women involved in MVC during any trimester of pregnancy. 8 out of 19 studies reported information
41 42	203	about the use of safety devices such as seatbelts and/or airbag (26, 29, 30, 33, 35, 37-39). Also in eight
43 44	204	studies, the authors assessed the severity of MVC injuries with five of these using a validated tool (28,
45 46	205	31, 35, 38, 42) – most of them reporting ISS (28, 31, 35, 42) and one the Revised Trauma Scale (38).
47 48	206	
49 50	207	Quality assessment
51 52	208	60% of studies had a low risk of bias with regards to the adequacy of representativeness and random
53 54	209	sample selection (12/19). None of the studies was prospective. The categories of follow up of more than
55 56	210	80% of participants, outcome ascertainment and misclassification bias showed low risk (Figure 2). The
57 58 59	211	five papers included for comparison of complication rates between pregnant women exposed to MVC
59 60	212	and those who were not exposed (assessed using the Newcastle-Ottawa Scale) showed generally high

quality, with four papers scoring 9/9 (6, 26, 28, 29). The remaining paper scored 8/9, losing one point
for the comparability as it did not control for any secondary factors (27).

#### 216 Incidence of complications among pregnant women involved in motor vehicle crashes

The assessment of adverse outcome incidence among women involved in MVC (using population-level data) demonstrated incidence estimations of 276.43 per 1000 for induction of labour (95% CI 262.54 to 290.54), 191.90 per 1000 for preterm delivery (95% CI 45.98 to 405.74), and 166.65 per 1000 for caesarean section (95% CI 47.34 to 339.00). The estimated incidence rates for other complications included 42.33 per 1000 for PROM, 17.08 per 1000 requiring admission to hospital, 16.14 per 1000 for placental abruption and 15.19 per 1000 for neonatal respiratory distress. A pooled incidence of maternal death was 3.60 per 1000 women (95% CI 0.25 to 10.42, 3 studies, 12,000 women, Tau=1.77). The pooled incidence of perinatal death (fetal death or stillbirth) per 1000 women was 6.60, (95% CI 3.81 to 10.12; 8 studies, 47,992 women; I<sup>2</sup>=92.6%) (Table 2). The representation of the maternal and offspring outcomes according to trauma severity are in appendices (Appendices 3 and 4). Using data from single hospital centres, the random pooled estimation for the incidence of admission to hospital was 117.92 per 1000 women (95% CI 109.82 to 126.40) (17, 38); for maternal death was 135.05 per 1000 women (95% CI 131.37 to 138.80) and for fetal death was 5.73 per 1000 women (95% CI 3.05 to 9.77) (Appendices 5 and 6).

232 Pregnancy complications in women involved vs not involved in motor vehicle crashes

We observed a statistically significant link between involvement in MVC and maternal death (OR 202.3, 95% CI 110.60 to 370.00; single study) (27) (data not shown in table or graphic). Figure 3 shows pooled results from population-level data, demonstrating a positive association between MVC and placental abruption (OR 1.43 95% CI 1.27 to 1.63). Two studies contributed data used in sensitivity analyses stratifying by seatbelt use, where the pooled estimation (26, 29) of fetal death decreased with seatbelt devices, but the association was not statistically significant (OR 0.66 95% CI 0.36 to 1.19) (Figure 1, supplementary). The review manager forest plot displays a positive but not statistically

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3 4	240	significant association between fetal death and MVC without seatbelt use (OR 5.78 95% CI 0.17 to
5 6	241	201.12, $Tau^2 = 6.51$ ) (Figure 2, supplementary).
7 8	242	
9 10	243	Discussion
11 12	244	Statement of principal findings
13 14 15	245	This review estimated that for women involved in MVC, maternal death occurrence was 3.6 per 1000
15 16 17	246	and perinatal death 6.6 per 1000 women. Compared to women not involved in MVC, those involved
18 19	247	had an increased odds of placental abruption, antepartum haemorrhage and maternal death. The pooled
20 21	248	incidence of complications per 1,000 women involved in MVC was, from the higher incidence to the
22 23	249	lower, induction of labour, preterm delivery, caesarean section, premature rupture of membrane, and
24 25	250	placental abruption (population level-data).
26 27	251	
28 29	252	Strengths and weaknesses of this study
30 31 32	253	This is the second systematic review, after the one of Mendez Figueroa et al., in 2013 (4), looking at
32 33 34	254	outcomes following MVC in pregnancy. We conducted our review using a prospectively registered
34 35 36	255	protocol (PROSPERO) and reported it in accordance with the international standards (43). This review,
37 38	256	to our best knowledge, is the first one examining the link between involvement in MVC, mortality and
39 40	257	adverse outcomes that involves evaluation of study quality assessment; 14 studies looking at outcome
41 42	258	incidence related to MVC (17, 30-42) and 5 studies comparing outcomes in pregnant women involved
43 44	259	in MVC and those who were not (6, 26-29). We used established tools to assess outcome reporting
45 46	260	quality for the incidence rates (44) and comparability (45). We included data from population-level and
47 48	261	single centre studies, but the analysis and reporting of the results were independent in order to get
49 50	262	precision and validity in the estimations. However, a couple of graphics of the maternal and offspring's
51 52	263	outcomes incidences have been included as Appendix 3 and 4. Between August 2018 and March 2020,
53 54 55	264	there have been no new studies eligible to include in the systematic review.
55 56 57	265	
57 58 59	266	For the incidence analysis, we evaluated the quality of the 19 studies of this systematic review. The

highest risk was in the design. None of the studies had a prospective design. The representativeness of

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cohort and the random method of sampling were other limitations of the quality of studies, with 7 out
of 19 studies having a high risk of bias in these areas (17, 31, 32, 35, 38, 39, 42). However, the quality
assessment of the five papers included for comparison of complication rates between pregnant women
involved and not involved in MVC using the Newcastle-Ottawa Scale showed generally high quality,
with four papers scoring 9/9 (6, 26, 28, 29).

The weaknesses of this systematic review are as follows. Firstly, outcomes were not reported by trimester, with 13 out of 19 papers focused on MVC at any trimester. Secondly, outcomes, according to seatbelt use, are scarce as only two studies using population-level data looked at safety features as a stratification factor (26, 29). Two studies with data sourced from hospital records/single-site trauma registries (38, 39) and three studies utilising population-level databases (26, 29, 30) reported some outcomes regarding seatbelt-use. Thirdly, we found a limited number of relevant studies comparing outcomes between women involved and not involved in MVC. The majority of the studies were carried out in the USA (26, 28, 29) with most recent one published in 2013 (29). Fourthly, the included studies differed in study design with seven of them using hospital records/single-site trauma registry (17, 31, 32, 35, 38, 39, 42) and twelve population database (6, 26-30, 33, 34, 36, 37, 40, 41). Despite analysing the data within the respective study designs and incorporation of anticipated variation into the statistical model (random-effects) (46), we encountered substantial statistical heterogeneity in the pooled estimates that could not be formally explored due to a limited number of studies and poor reporting of important factors such as trauma severity. As a fifth point, these data apply to developed countries - only one of the papers included data from an underdeveloped country, perhaps influencing the outcomes that might otherwise be seen in the developed world. Finally, in only eight studies did authors assess severity of MVC injuries, with only five of these using a validated tool (28, 31, 35, 38, 42). This was a challenge when aiming to analyse results according to the severity of the crash.

*Meaning of the study* 

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The strongest association was found between placental abruption (6, 28, 29) and MVC. Maternal death was associated with involvement in MVC but this finding needs to be treated with caution as the data come from a single study (27). The outcomes in descending order of incidence estimate per 1000 (population-level data) were the induction of labour, preterm delivery, caesarean section, premature rupture of membranes, and admission to hospital, placental abruption and maternal death. In the analyses stratified by use of seatbelt, we observed an association of fetal death with lack of seatbelt use by pregnant women involved in an MVC. However, this finding was not statistically significant and informed by a limited number of studies. Previous studies have shown that pregnant women wearing seatbelt during the MVC did not experience a significantly higher risk of adverse fetal outcomes than women who were not involved in MVC (47) Furthermore, airbags seem to be contributing to the protection of both pregnant drivers and their fetuses (48).

The results of this systematic review provide evidence informing primary prevention measures, recommendations and educational interventions for pregnant women in the context of MVC that should be incorporated into the primary care guidelines. 

#### Unanswered questions and future research

The effects of MVC in pregnant women is a specific field that requires further research and an improved methodological approach to determine the risks of adverse maternal and fetal outcomes. 

Additional variables such as trauma severity, the position of the women in the car, use of seatbelt, deployment or non-deployment of an airbag, severity of the crash and gestational week of pregnancy should be recorded in relation to MVC exposure in order to allow more precision when analysing outcomes. A greater number of well-designed studies in a variety of global settings would strengthen current evidence-base.

*Conclusions* 

Pregnant women involved in MVC seem to be at increased risk of maternal death and complications, especially placental abruption, than those not involved in MVC. The risk of complications such as preterm delivery, premature rupture of membranes and caesarean section were also increased. However,

2		
3 4	323	these findings need to be treated with caution due to the small number of studies included in the review
5 6	324	and considerable differences between studies. Road traffic authorities should be conscious and strict in
7 8	325	targeting preventive measures aimed at pregnant users of motor vehicles due to risk associated with
9 10	326	potential involvement in MVC.
11 12	327	
13 14	328	Word count: 3,147
14 15 16	329	
17 18	330	Author's contribution
19 20	331	PM conducted literature searches and screened publications jointly with JR. CAP and JR extracted the
20 21 22	332	data. CAP and ER drafted the manuscript and conducted the statistical analyses. KSK and ST designed
22 23 24	333	the study review. CAP is the guarantor. Authors VMR, KB, ABC, ST and KSK gave critical revision
25		
26 27	334	of the manuscript. All authors had full access to the data and take responsibility for the data analyses.
28 29	335	The corresponding author attests that all listed authors meet authorship criteria.
30	336	
31 32	337	Acknowledgement
33 34	338	Professor Khalid S. Khan is distinguished investigator at the University of Granada through a Beatriz
35 36 27	339	Galindo (Senior Modality) Program grant of the Spanish Ministry of Science, Innovation and
37 38	340	Universities.
39 40	341	
41 42	342	Data sharing Statement
43 44	343	All data relevant to the study are included in the article or uploaded as supplementary information
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 Table 1. Characteristics of included studies

Study ID Author, year, Country	Design	Sample size	Time period	Inclusion criteria	Data source	Trimester	Seatbelt use (with data)	Assessment of trauma severity (with data)	Method of assessing trauma severity	Maternal outcomes	Offspring outcomes
Population-leve	el data										
<b>Azar, 2005</b> USA	population-based matched retrospective cohort (incidence only)	5936	2003- 2011	Admitted to hospital following MVC while pregnant	Population-based cohort	any	no	no	N/A	Maternal death	
<b>Hyde, 2003</b> USA	retrospective cohort (incidence and comparison)	322704	1992- 1999	Pregnant drivers involved in MVC	Linked databases (police registry & birth/death certificates)	any	yes	yes	Study- specific definition <sup>1</sup>		Fetal death
Kvarnstrand, 2008 Sweden	retrospective cohort (incidence and comparison)	1094559	1991- 2001	Maternal inclusion on the accident register > 28 GW	Linked databases (police registry & birth/death certificates)	2 <sup>nd</sup>	no	yes	Study specific definition <sup>2</sup>	Maternal death	Fetal/neonatal death
<b>Kuo, 2007</b> USA	retrospective chart/database review (incidence only)	16982 injuries 4479 (in MVC)	2002	Pregnant women hospitalized with injury (only MVC used)	Sample from population level cohort (National Inpatient Sample)	any	no	no	N/A	Delivery, hospitalization	
<b>Schiff, 2005</b> USA	retrospective cohort (incidence and comparison)	17899	1989- 2001	Hospitalized for MVC and with a singleton livebirth or fetal death	Linked databases (hospital discharge data & birth/death certificates)	any	no	yes	ISS	Preterm birth, PROM, C-section, placental abruption	Stillbirth LBW, SGA, Fetal distress, RDS, Meconium
<b>Schiff, 2010</b> USA	retrospective cohort (incidence only)	3348	2002- 2005	Non-rollover MVC among pregnant front seat occupants	Linked databases (hospital discharge data & birth/death certificates)	any	yes (airbag) no (seatbelt)	no	N/A	Preterm birth, placental abruption, labour induction, C- section	Stillbirth, LBW SGA, RDS Fetal distress Meconium
<b>Vivian-</b> <b>Taylor, 2012</b> Australia	retrospective cohort (incidence and comparison)	604380	2000- 2007	Women who gave birth exposed and not exposed to MVC	Linked databases (hospital discharge data & birth/death certificates)	2 <sup>nd</sup>	no	yes	Study- specific definition <sup>3</sup>	Admission, placental abruption, APH, PPH, preterm birth, C-section	Perinatal death (>20 <sup>th</sup> GW), neonatal transfer

Vladutiu, 2013 USA	retrospective cohort (incidence and comparison)	878546	2001- 2008	Pregnant women 16-46 years, > 20GW, delivering a live/ stillbirth singleton infant	Linked databases (police registry & birth/death certificates)	2 <sup>nd</sup>	yes (seatbelt) yes (airbag)	no	N/A	Placental abruption, PROM, preterm birth	Stillbirth
<b>Weiss, 2002</b> USA	crash database pregnant vs. non- pregnant (NASS/CDS) <i>(incidence only)</i>	32810	1995- 1999	Pregnant and non- pregnant women 15–39 years	Sample from population-level database of traffic accidents	any	yes	no	N/A	Maternal death	
Weiss, 2008 USA	retrospective cohort (incidence only)	1816	1999- 2002	Injury-related emergency department visits by pregnant women (only MVC used)	Linked databases (hospital discharge data & birth/death certificates)	any	no	no	N/A	Hospital admission	
Whitehead, 2013* USA	PRAMS survey database (incidence only)	235329	2000- 2005	Survey of women who recently delivered a live- born infant	Population-based cohort (PRAMS)	any	no	no	N/A	Preterm birth, UTI, PROM	
<b>Wolf, 1993</b> USA	population-based retrospective cohort (incidence only)	2582	1980- 1988	Pregnant women drivers involved in MVC >20GW	Linked databases (police registry & birth/death certificates)	2 <sup>nd</sup> & 3 <sup>rd</sup>	yes	no	N/A	Preterm birth, placental abruption, C-section	Stillbirth, LBW, RDS
Single hospita	l records/trauma reg	istry									
<b>Aboutanos,</b> 2007 USA	retrospective chart/database review (incidence only)	148	2001- 2005	Pregnant women presenting to ED following MVC	Single hospital records from trauma centre	any	yes (only in miscarriage)	yes	ISS	Maternal death, miscarriage	Fetal death hydrops fetalis
Baerga- Varela, 2000 USA	retrospective chart/database review (incidence only)	39	1986- 1996	Admitted to hospital after MVC while pregnant	Single hospital records	any	no	yes	ISS	Maternal death, miscarriage	Stillbirth
<b>Brookfield,</b> 2013 USA	retrospective chart/database review (incidence only)	256	1990- 2007	Pregnant women presenting to ED following MVC	Single hospital records from trauma centre	any	yes	yes	ISS and RTS	Maternal death, admission to hospital	

Chibber,	retrospective	728	2009-	MVC, pregnant,	Single hospital	2 <sup>nd</sup>	no	no	N/A	Maternal death,	Fetal death,
2015 Kuwait	chart/database review (incidence only)		2012	treated at major tertiary hospitals	records					placental abruption, preterm birth, uterine rupture, C-Section, admission	fetal distres
Luley, 2013 USA	retrospective chart/database review (incidence only)	126	1994- 2010	Pregnant women after an MVC >14/40 GA	Single hospital trauma database	2 <sup>nd</sup> & 3 <sup>rd</sup>	yes	no	N/A	Maternal death, placental abruption, C-section	Stillbirth
<b>Miller, 2016</b> Israel	retrospective cohort (incidence only)	3794	2006- 2013	Women 18-40 years, in MVC and hospitalized (only pregnant cohort used)	National trauma registry	any	no	no	ISS	Maternal death, miscarriage, placental abruption, C-section	Stillbirth
<b>Orji, 2002</b> Nigeria	retrospective chart/database review (incidence only)	84	1980- 2000	Pregnant women in MVC managed in tertiary hospitals	Single hospital records**	any	no	no	N/A	Maternal death, placental abruption, uterine rupture, C-section	Perinatal death (fetal death), feta tachycardia

ISS: Injury Severity Score; RTS: Revised Trauma Score; ICU: Intensive Care Unit, N/A not applicable; GA: Gestational Age; LBW: Low birth weight; SGA: Small for gestational age; RDS: Respiratory distress syndrome. \*National survey; \*\*Two hospitals in same region included; <sup>1</sup>Possible/probable/incapacitated/fatal; <sup>2</sup>Fatal/major/minor/uninjured; <sup>3</sup>'Severe' = admission to ICU and/or blood transfusion and/or injury to abdomen/pelvis/lower back.

Table 2. Incidence of adverse outcomes per 1,000 women involved in motor vehicle crashes.

Outcome and study	Number of studies	Number of women	Incidence estimate per 1,000 women	95% CI
Maternal				
Maternal death	3	12000	3.60	(0.25 to 10.42)
Azar, 2005		+	6.57	(4.68 to 8.97)
Kvarnstrand, 2008			6.61	(3.70 to 10.88)
Miller, 2016			0.26	(0.01 to 1.47)
Admission to hospital	2	3838	17.08	(13.20 to 21.46)
Vivian-Taylor, 2012	'n		8.90	(5.28 to 14.03)
Weiss, 2008	~		29.19	(21.94 to 38.0)
Placenta abruption	6	36737	16.14	(7.04 to 28.78)
Wolf, 1993			8.10	(5.02 to 12.36)
Miller, 2016	9		1.05	(0.29 to 2.70)
Schiff, 2005			113.40	(88.80 to 142.01)
Schiff, 2010			12.25	(8.80 to 16.58)
Vivian-Taylor, 2012		- 4,-	16.32	(11.26 to 22.84)
Vladutiu, 2013			7.17	(6.15 to 8.31)
Preterm delivery	5	265680	191.90	(45.98 to 405.74)
Schiff, 2005			316.15	(278.53 to 355.65)
Schiff, 2010			97.37	(87.53 to 107.92)
Vivian-Taylor, 2012		+	83.09	(71.42 to 95.98)
Vladutiu, 2013		++	110.33	(106.43 to 114.33)
Whitehead, 2013	 	++	437.00	(435.00 to 439.01)
PROM	3	260310	42.33	(5.87 to 109.24)
Schiff, 2005		+	22.34	(11.95 to 37.89)
Vladutiu, 2013		+	23.53	(21.66 to 25.51)
Whitehead, 2013		++	96.00	(94.81 to 97.20)
Labour induction	2	3930	276.43	(262.54 to 290.54)

Schiff, 2005			223.37	(190.15 to 259.42)
Schiff, 2010			286.14	(270.87 to 301.78)
Caesarean section	5	12338	166.65	(47.34 to 339.00)
Miller, 2016			6.06	(3.85 to 9.08)
Schiff, 2005			254.30	(219.38 to 291.73)
Schiff, 2010			259.26	(244.48 to 274.46)
Vivian-Taylor, 2012			260.14	(241.13 to 279.85)
Wolf, 1993			171.68	(157.35 to 186.76)
Offspring		I		
Perinatal death	8	47992	6.60	(3.81 to 10.12)
Kvarnstrand, 2008	fetal/neonatal		17.62	(12.62 to 23.92)
Hyde, 2003	fetal		5.01	(3.66 to 6.70)
Miller, 2016	stillbirth		0.79	(0.16 to 2.31)
Schiff, 2005	fetal		12.03	(4.85 to 24.62)
Vivian-Taylor, 2012	stillbirth		16.82	(11.67 to 23.42)
Vladutiu, 2013	stillbirth		5.25	(4.38 to 6.23)
Schiff, 2010	fetal		4.18	(2.29 to 7.01)
Wolf, 1993	fetal	2	3.47	(1.59 to 6.58)
Fetal distress	2	3930	60.09	(52.85 to 67.77)
Schiff, 2005			132.30	(105.84 to 162.56)
Schiff, 2010			50.48	(43.31 to 58.44)
Meconium at delivery	2	3930	52.61	(45.82 to 59.85)
Schiff, 2005			63.57	(45.15 to 86.57)
Schiff, 2010			51.08	(43.86 to 59.08)
RDS	3	6522	15.19	(5.83 to 28.68)
Schiff, 2005			32.65	(19.77 to 50.51)
Schiff, 2010			14.64	(10.85 to 19.30)
Wolf, 1993			6.17	(3.53 to 10.00)

**Data source: population database**; CI, Confidence Interval; PROM: Premature Rupture of Membranes; RDS: Respiratory Distress Syndrome.

#### **Figures**

Figure 1. The study selection process in the systematic review of outcomes on pregnant women involved in motor vehicle crashes

Figure 2. The quality assessment of the included studies

Figure 3. Comparison of outcomes between women involved and not involved in motor vehicle crashes

Figure 1. (Supplementary). Comparison of pregnancy complications between women involved and not involved in motor vehicle crashes stratified by seatbelt use

Figure 2. (Supplementary). Comparison of fetal death between women involved and not involved in motor vehicle crashes stratified by seatbelt use

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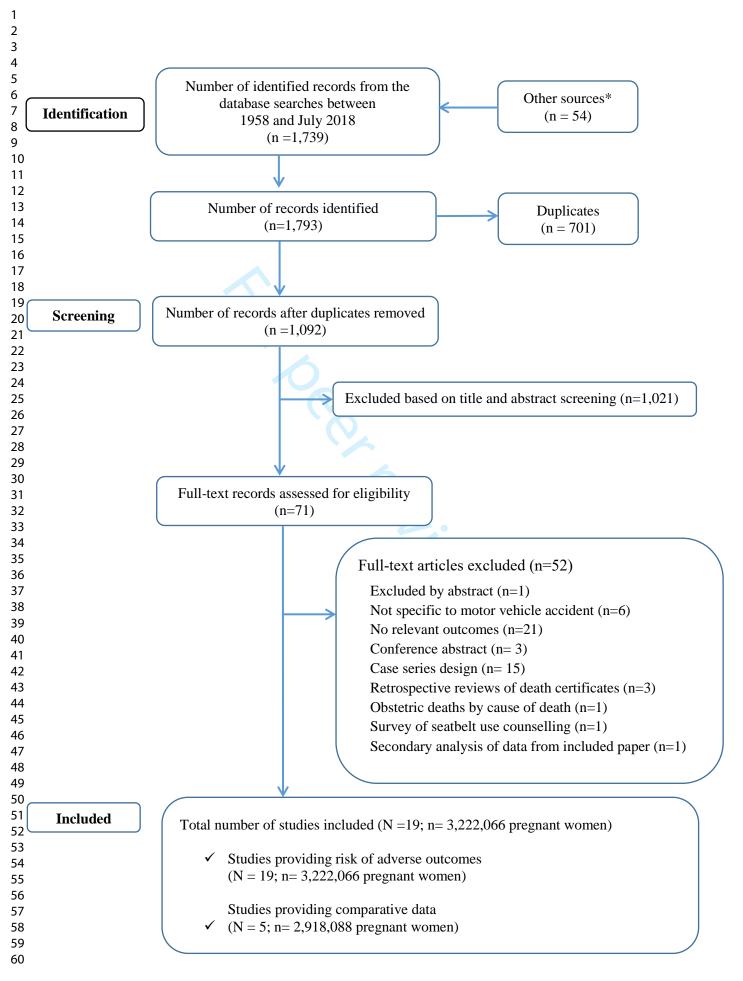
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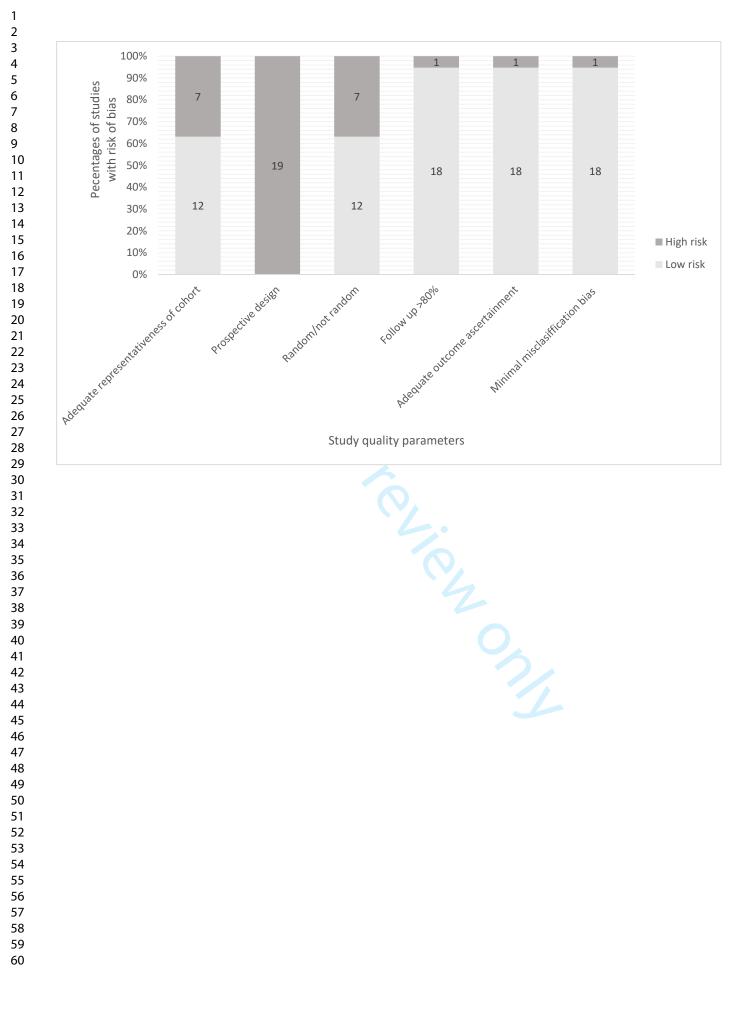
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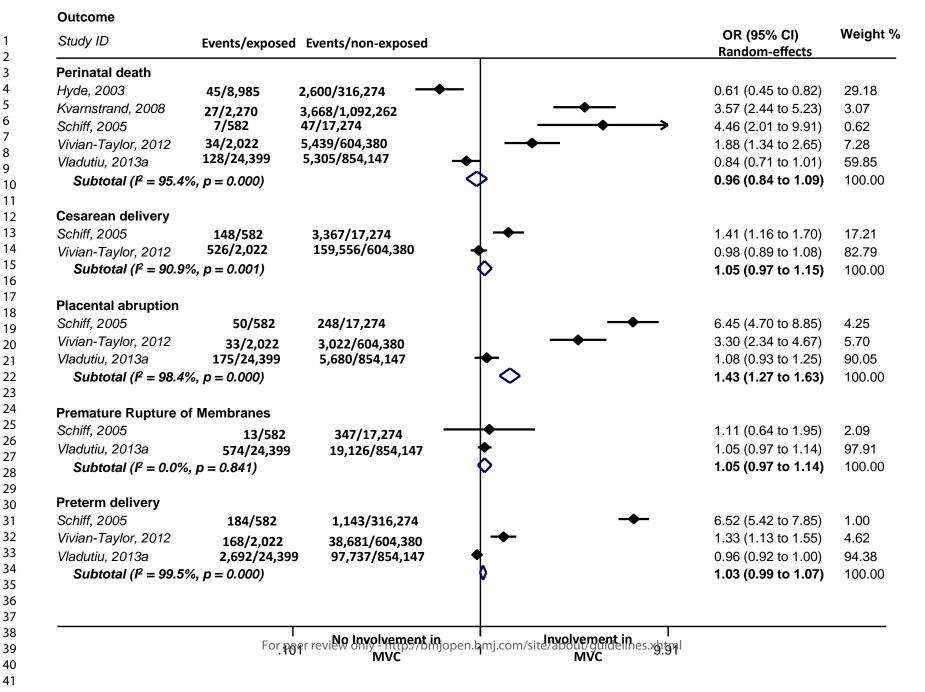
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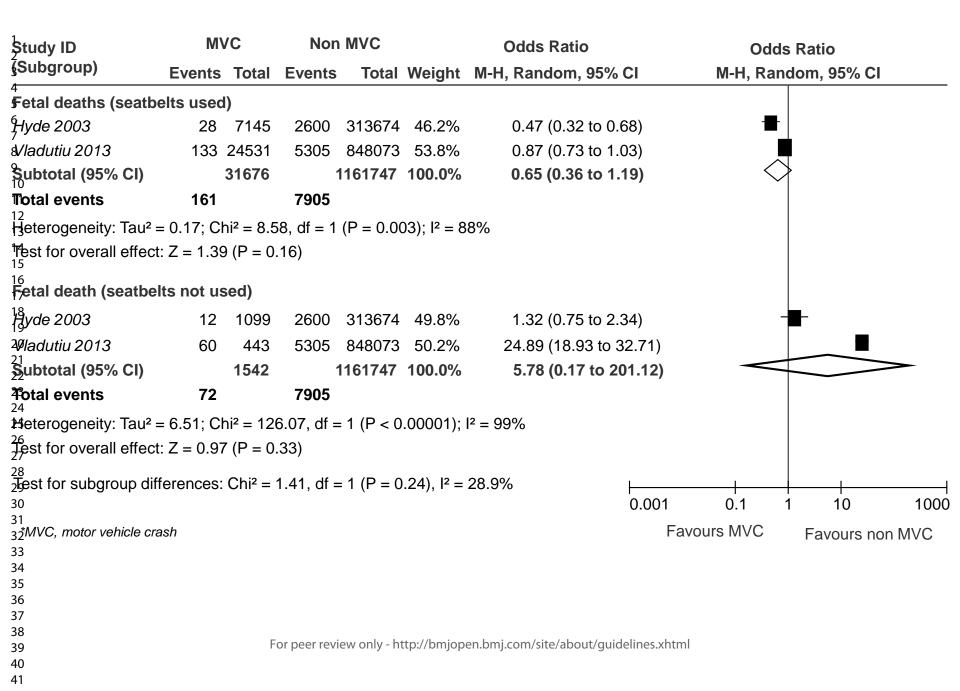
\*references of relevant non-systematic reviews and Google scholar



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Pa	ge 27 of 38 <b>Outcome</b>	• •			BMJ Open	
1	Study ID	Overall incidence	Study size			OR (95% CI)
2	Fetal death					
4 5	Seatbelts not u	sed				
6	Hyde, 2003	1.176	2222		_ <b>+</b>	1.32 (0.74 to 2.33)
7 8	Vladutiu, 2013a	5.333	1006			→ 21.65 (16.51 to 28.39)
9 10	Seatbelts used					
11	Hyde, 2003	.1832	14346		- <b>-</b> -	0.47 (0.33 to 0.69)
12 13	Vladutiu, 2013a	.1102	49328		•	0.87 (0.73 to 1.03)
14 15						
16 17		sed				
18	Vladutiu, 2013a	.1152	49328	← ◆	—	0.02 (0.01 to 0.06)
19 20						
21 22	Vladutiu, 2013a	.1188	49328		•	1.09 (0.93 to 1.26)
23						
24 25	Seatbelts not u					
26		97.2	1006		-	0.85 (0.64 to 1.14)
27 28						
29	Vladutiu, 2013a	2.035	49328		•	0.94 (0.90 to 0.97)
30 31	Premature Rupture	Of Membran	es			
32 33		sed				
34		.388	49328			0.02 (0.01 to 0.04)
35 36						
37 38		.3993	49328	1 1 74	• • • • • • • • • • •	1.03 (0.95 to 1.12)
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9	childbearing.af.				
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29	car collision*.af.				
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	27 or 28 or 29 or 30 or 31 or 32 or 33 or 34 or 35				
38	36 and 37				

Appendix 1. Search strategy for MEDLINE (via Ovid) executed from database inception up to July 2018

Appendix 2 List of excluded studies with reasons
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Study ID	Reason	Reference	
Al Mulhim, 2012	Pregnancy loss or not after trauma in Arabic pregnant women	EMHJ. Vol. 18 No. 5 2012	
Battaloglu 2016	From a cohort of 15,140 female patients, 173 were pregnant women in the trauma registry. 55.5% of them from vehicle collision	SR Petrone, 2017 Injury, Int. J. Care Injured 47 (2016) 184-187	
Barre 2006	Pregnant women with abdominal trauma during pregnancy (n=65). Half of them from a traffic accident.	<b>SR Petrone, 2017</b> La Revue Sage-Femme. Vol 5, Issue 6, 2006, 312-316	
Cannada 2010	Pregnant women with orthopaedic injuries (n=65)	SR Petrone, 2017 Injury, Infection, and Critical Care.2010. Vol. 69 (3)	
Chamberlain, 2011	Communication abstract. Retrospective cohort study. Identification of 272 pregnant trauma victims. 78.6% of them incurred in a MVC. No data to extract	American Journal of Obstetrics & Gynecology Supplement to January 2011	
Cheng, 2012	Maternal complications during delivery according to uninjured, minor and severe injuries. 2,881 pregnant women (47,4%) involved in MVC	World J Surg (2012) 36:2767– 2775	
Connolly, 1997	476 maternal records of trauma cases. 54.6% were MVC. No more data available	American Journal of Perinatology.1997.Vol. 14 (6)	
Corsi 1999	Twenty-seven traumatised pregnant women were analysed retrospectively over a period of 9 years in Sao Paulo, Brazil	SR Petrone, 2017 Injury, Int. J. Care Injured 30 (1999) 239-243	
Dannenberg, 1995	Homicide and other injuries as causes of maternal death between 1987 and 1991 in New York	Am J Obstet Gynecol Vol.172 (5)	
Deshpande, 2017	Trauma impact on maternal mortality. Comparability between pregnant vs. non pregnant women	American Journal of Obstetrics & Gynecology 2017. 590.e2	
El Kady 2004	Retrospective cohort study of women hospitalized for Trauma in California	SR Petrone, 2017 American Journal of Obstetrics and Gynecology (2004) 190, 1661-8	
El Kady D, 2006	Fractures injuries on maternal/neonatal outcomes in United States	SR Méndez -Figueroa 2013 American Journal of Obstetrics and Gynecology (2006) 195, 711–6	
Fischer 2011	Minor trauma and poor fetal outcomes in Tennessee, Memphis	SR Petrone, 2017 Injury, Infection, and Critical Care. 2011. Vol. 71 (1)	
Gibbins, 2017	Communication. MVC and Stillbirth. Secondary analysis of 439 stillbirth	American Journal of Obstetrics & Gynecology Supplement to January 2017	
Goodwin, 1990	Case-series of trauma pregnant women between 1987 and 1988 in Los Angeles	SR Méndez -Figueroa 2013 Am J Obstet Gynecol. 1990 Vol. 162 (3).	
Hardt, 2013	Prenatal risk screening to identify women at increased risk for traumatic pregnancy-	Women's Health Issues 23-3 (2013) e187–e193	

	associated death		
Hardy, 1974	Maternal mortality ratios at large urban	Obstetric and Gynecology.	
	charity hospitals from 1941 to 1971	1974. Vol.43 (1)	
Harland 2014	Risks factors of maternal injuries in a	SR Petrone, 2017	
	population-based sample of pregnant women	Journal of Women's Health.	
	from Iowa	2014. Vol. 23 (12)	
Hitosugi 2006	135 traffic accidents involving Japanese	SR Petrone, 2017	
	pregnant women from insurance companies.	Forensic Science International	
	The outcomes of neonates determined by	159 (2006) 51-54	
	their condition 1 month after birth		
	(death/abortion/healthy)		
Ikossi, 2005	Risks factors of trauma in pregnant women	J Am Coll Surg. Vol. 2005. 200	
	from San Francisco, California	(1)	
Lynch, 2011	Pregnancy associated- death in Ohio: 2003-	American Journal of Obstetric	
	2007	& Gynecology Supplement to	
		January 2011	
Manoogian, 2015	Injuries characteristics between pregnant vs	Accident Analysis and	
	non pregnant women occupants (not	Prevention 74 (2015).	
	outcome)	69–76	
Melamed 2012	Outcomes following blunt trauma in Pregnant	SR Petrone, 2017	
	women from Israel	The Journal of Maternal-Feta	
		and Neonatal Medicine. 2012	
		25(9): 1612–1617	
Mesdaghinia, 2012	Causes of trauma in 32 pregnant women with	Arch Trauma Res.	
	trauma in a Hospital in Iran	2012;1(1):23-26	
Nannini, 2008	Risks of injury in pregnant women in	Journal of Midwifery &	
	Massachusets	Women's Health.2008. Vol.53	
		(1)	
Omoke, 2013	Trauma during pregnancy in a Nigerian	Int J Crit Illn Inj Sci. 2013; 3(4)	
· · · · · · · · · · · · · · · · · · ·	setting	269–273.	
Osei-Ampofo, 2016	A cross-sectional study with 134 pregnant	African Journal of Emergency	
	women from Ghana visiting the emergency	Medicine (2016) 6, 87 –93	
	care. Leading injury MVC (23%). Not		
<b>D</b>   4000	outcomes		
Pak, 1998	Delivery outcomes after a blunt abdominal	Am J Obstet Gynecol. 1998.	
Detteren 2007	trauma in 85 pregnant women	Vol. 179 (5)	
Patteson, 2007	High risk factors involved in trauma during	The Journal of TRAUMA Injury	
	pregnancy. Not outcomes	Infection, and Critical Care.	
Dearline ( 1000	Not possible to process full taut	2007. Vol 62 (4)	
Pearlman, 1990	Not possible to assess full text	SR Méndez -Figueroa 2013	
Schiff, 1997	Seat Bealt use. Protective factor of maternal	WJM, 1997. Vol. 167 (1)	
,	mortality after a MVC in Mexico	,	
Schuster, 2016	Communication abstract. Impact of blunt	American Journal of Obstetric	
	trauma on maternal and pregnancy outcome.	& Gynecology. Supplement to	
	MVC the most common injury mechanism	January 2016	
	(70%). Pennsylvania Trauma Systems	,	
	Foundation Database (1996-2013).		
Schuster, 2018	Pennsylvania Trauma Systems Foundation	Trauma, 2018. Vol. 20(1) 30–.	
	Database. ISS>9 and SBP<90mmHg are		
	predictors for poor outcomes after trauma		
	during pregnancy		
Sela, 2011	Treatment provided to pregnant motor	Annals of Surgery,	
	vehicle accident (MVA) casualties in a mature	2011.Vol.254 (2)	
	trauma system in Israel		

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Shah, 1998	Trauma in general in pregnant women	J Trauma. 1998 Jul;45(1):83-6	
Shakerian 2015	Determining adherence to recommended	SR Petrone, 2017	
	imaging guidelines in pregnant women from	J Trauma Acute Care Surg.	
	Victoria, Australia	2015.Vol. 78 (1)	
Shiff 2002	Retrospective cohort study to assess	SR Petrone, 2017	
	outcomes of pregnant women hospitalized	J Trauma. 2002; 53: 939–945.	
	for injury in Washington State from 1989 to		
	1997		
Sirin, 2007	Report the prevalence of seatbelt counselling	Matern Child Health J (2007)	
	by prenatal care providers during pregnancy	11:505–510	
	in USA		
Tinker 2010	Risks factors involved in injuries in pregnant	SR Petrone, 2017	
	women from the National Birth Defects	Journal of Women's Health.	
	Prevention Study, USA	2010. Vol. 19 (2)	
Van der Knoop, 2015	Effect of maternal trauma in fetal motility at	Early Human Development 91	
• •	term and at one year of age	(2015) 511–517	
Van der Knoop, 2018	Matched case-control study. Neurobehavioral	European Journal of Paediatric	
• •	outcome in 6-18 year old children after	Neurology (2018), 22(5):845-	
	trauma in pregnancy	853	
Vladutiu, 2013b	Same sample Vladutiu 2013a; excluded as a	Accid Anal Prev. 2013; 55: 165-	
	secondary analysis from already included	171	
	study		
Wahabi, 2007	45 MVC case series pregnant women	Saudi Med J. 2007. Vol. 28 (9)	
	collected over a 10- year period		
Wall 2014	Pregnant trauma patiens from South Africa	SR Petrone, 2017	
	(mainly assaults)	Injury, Int. J. Care Injured	
		45 (2014) 1220–1223	
Weiner 2016	Minor trauma during pregnancy, not	SR Petrone, 2017	
	associated with adverse pregnancy outcomes,	European Journal Of Obstetrics	
	Israel	& Gynecology	
		and Reproductive Biology	
	4	203 (2016): 78–81	
Weiss, 1999	Retrospect review of death certificates	43rd Annual Proceedings	
		Association for the	
		Advancement of Automotive	
		Medicine September 20-21,	
	•	1999. Barcelona (Sitges), Spain	
Weiss, 2001	Retrospect review of death certificates	JAMA, 2001. Vol. 286 (15)	
Weiss, 2002a	N/A		
Zangene, 2015	102 cases of trauma in pregnancy registered	Global Journal of Health	
<b>U</b> , -	in Iran from 2007 to 2010. MVC the most	Science. 2015. Vol 7 (2)	
	frequent (45%)		
		1	

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# maternal outcomes

2	1		
3 4	Study	ES (95% CI)	Trauma_severity
5	Placental abruption	I	
6	Wolf, 1993	8.10 (5.02, 12.36)	NK
7	Miller, 2016	1.05 (0.29, 2.70)	NK
8	Schiff, 2005	130.95 (67.22, 222.24)	severe
9	Schiff, 2005		mild
10	Schiff, 2005	127.23 (95.92, 164.27)	mild-severe
11 12	Schiff, 2010	12.25 (8.80, 16.58)	mild
12	Vivian-Taylor, 2012	16.32 (11.26, 22.84)	mild-severe
13	Vladutiu, 2013a	7.17 (6.15, 8.31)	NK
14 15	Subtotal (I <sup>2</sup> = 96.7%, p = 0.00	15.41 (9.52, 21.30)	
15 16		10.11 (0.02, 21.00)	
16 17	Admission to hospital		
18	Vivian-Taylor, 2012	8.90 (5.28, 14.03)	mild-severe
19	Weiss, 2008	29.19 (21.94, 38.00)	NK
20	Subtotal (I <sup>2</sup> = .%, p = .)	13.33 (9.72, 16.95)	
20		13.33 (3.72, 10.33)	
22	Cesarean delivery		
23	Miller, 2016	6.06 (3.85, 9.08)	NK
24	Schiff, 2005	309.52 (213.14, 419.80)	
25	Schiff, 2005	249.19 (201.95, 301.31)	
26	Schiff, 2005		
27	Schiff, 2010	259.26 (244.48, 274.46)	
28	Vivian-Taylor, 2012	260.14 (241.13, 279.85)	
29	Wolf, 1993	<b>171.68 (157.35, 186.76)</b>	
30	Subtotal (I^2 = 99.7%, p = 0.00		INIX
31	Subtotal ( $1^{-2} = 99.7\%$ , p = 0.00	215.33 (97.40, 333.26)	
32	Leber induction		
33	Labor induction		
34	Schiff, 2005		severe
35	Schiff, 2005		
36	Schiff, 2005		
37	Schiff, 2010		mila
38	Subtotal (I^2 = 87.0%, p = 0.00	228.25 (173.87, 282.63)	
39		The second s	
40	Maternal death		N117
41	Azar, 2005	6.57 (4.68, 8.97)	NK
42	Kvarnstrand, 2008	6.61 (3.70, 10.88)	mild-severe
43	Miller, 2016	0.26 (0.01, 1.47)	NK
44	Subtotal (I^2 = .%, p = .)	4.34 (-0.72, 9.41)	
45		The second s	
46	Premature Rupture of Membranes		
47	Schiff, 2005	11.90 (0.30, 64.55)	severe
48	Schiff, 2005	22.65 (9.16, 46.12)	mild
49	Schiff, 2005	20.36 (8.83, 39.71)	mild-severe
50	Vladutiu, 2013a	23.53 (21.66, 25.51)	NK
51	Whitehead, 2013	<b>95.72 (76.16, 118.34)</b>	NK
52	Subtotal (I^2 = 91.8%, p = 0.00	34.09 (13.89, 54.29)	
53			
54	Heterogeneity between groups: p = 0.000		
55	Overall (I^2 = 99.45%, p = 0.00;	••       75.74 (68.25, 83.24)	
56			
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58	7023	420	
59 60			
60	For	peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml	

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Study		ES (95% CI)	Trauma
Fetal death			
Kvarnstrand, 2008		11.89 (7.85, 17.26)	mild-sev
Schiff, 2010		4.18 (2.29, 7.01)	mild
Wolf, 1993		3.47 (1.59, 6.58)	NK
Subtotal (I <sup>2</sup> = .%, p = .)	<b>6</b> •	5.98 (2.16, 9.79)	
(1270, p)	<b>*</b> •	0.00 (2.10, 0.10)	
Fetal distress			
Schiff, 2005		202.38 (122.54, 304.14)	severe
Schiff, 2005		119.74 (85.73, 161.25)	mild
Schiff, 2005		137.40 (104.94, 175.45)	mild-sev
Schiff, 2010		50.48 (43.31, 58.44)	mild
Subtotal (I^2 = 93.6%, p =	0.00)	119.86 (57.95, 181.77)	
	0.007		
Meconium at delivery			
Schiff, 2005		59.52 (19.61, 133.47)	severe
Schiff, 2005		48.54 (27.42, 78.80)	mild
Schiff, 2005		50.89 (31.36, 77.50)	mild-sev
Schiff, 2010		51.08 (43.86, 59.08)	mild
			miu
Subtotal $(I^2 = 0.0\%, p = 0)$	0.99)	51.01 (44.30, 57.71)	
Perinatal death			
Kvarnstrand, 2008		101.50 (67.96, 144.24)	severe
Kvarnstrand, 2008		8.93 (4.77, 15.23)	mild
Kvarnstrand, 2008		17.62 (12.62, 23.92)	mild-sev
		5.01 (3.66, 6.70)	NK
Hyde, 2003	E 1		
Miller, 2016	T _ 1	0.79 (0.16, 2.31)	NK
Schiff, 2005		23.81 (2.90, 83.37)	severe
Schiff, 2005		16.18 (5.27, 37.36)	mild
Schiff, 2005		17.81 (7.19, 36.35)	mild-sev
Vivian-Taylor, 2012		16.82 (11.67, 23.42)	mild-sev
Vladutiu, 2013a		5.25 (4.38, 6.23)	NK
Schiff, 2010		4.18 (2.29, 7.01)	mild
Wolf, 1993		3.47 (1.59, 6.58)	NK
Subtotal (I^2 = 92.3%, p =		8.06 (5.36, 10.76)	
oubtotal (1 2 - 52.570, p -	0.007		
Preterm delivery	1 - E		
Schiff, 2005		130.95 (67.22, 222.24)	severe
Schiff, 2005	1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1	245.95 (198.96, 297.89)	mild
Schiff, 2005	1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1	221.37 (181.29, 265.71)	mild-sev
Schiff, 2010		97.37 (87.53, 107.92)	mild
Vivian-Taylor, 2012		<b>83.09</b> (71.42, 95.98)	mild-sev
Vladutiu, 2013a		■ 110.33 (106.43, 114.33)	NK
Whitehead, 2013	1	435.77 (400.94, 471.07)	NK
Subtotal (I^2 = 98.6%, p =	0.00)	187.07 (141.39, 232.74)	
Poppiratory distrace average			
Respiratory distress syndro			
Schiff, 2005		59.52 (19.61, 133.47)	severe
Schiff, 2005		22.65 (9.16, 46.12)	mild
Schiff, 2005		30.53 (15.88, 52.73)	mild-sev
Schiff, 2010		14.64 (10.85, 19.30)	mild
Wolf, 1993		6.17 (3.53, 10.00)	NK
Subtotal (I <sup>2</sup> = 82.4%, p =	0.00)	16.56 (7.94, 25.19)	
Heterogeneity between gro			
Overall (I^2 = 99.27%, p =	0.00);	49.67 (42.57, 56.76)	

Total sample size	Incidence estimate per 1,000 women (95%CI)
\$	
235329	100.00 (98.79, 101.22)
3794	1.85 (0.74, 3.80)
2022	47.48 (38.62, 57.67)
2022	77.65 (66.35, 90.18)
235329	247.00 (245.26, 248.75)
5936	117.92 (109.82, 126.40)
32810	135.05 (131.37, 138.80)
1	
582	22.34 (11.95, 37.89)
2270	5.73 (3.05, 9.77)
2022	42.53 (34.16, 52.26
	s 235329 3794 2022 2022 235329 5936 32810 1 1 582 2270

Appendix 5. Incidence of maternal, fetal & neonatal complications from single studies

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Outcome	Study ID	Number of events	Group size	Trauma severity level
Admission to hospital	Brookfield, 2013	182	256	Not given
	Chibber, 2015	648	728	Not given
Caesarean delivery	Chibber, 2015	529	728	Not given
	Luley 2013	32	126	Not given
	Orji, 2002	2	84	Not given
Fetal death	Aboutanos, 2007	1	148	Not given
	Chibber, 2015	78	728	Not given
Fetal distress	Chibber, 2015	412	728	Not given
Fetal tachycardia	Orji, 2002	10	84	Not given
Hydrops fetalis	Aboutanos, 2007	1	148	Not given
Maternal death	Aboutanos, 2007	0	148	Not given
	Baerga-Varela, 2000	1	39	Severe
	Brookfield, 2013	7	256	Not given
	Chibber, 2015	100	728	Not given
Maternal death	Orji, 2002	2	84	Not given
Miscarriage	Aboutanos, 2007	5	148	Not given
	Baerga-Varela, 2000	7	39	Mild to severe
Perinatal death	Baerga-Varela, 2000	23	39	Mild to severe
	Luley 2013	6	126	Not given
	Orji, 2002	3	84	Not given
Placental abruption	Chibber, 2015	428	728	Not given
	Luley 2013	7	126	Not given
	Orji, 2002	1	84	Not given
Preterm delivery	Chibber, 2015	97	728	Not given
Uterine rupture	Chibber, 2015	12	728	Not given
	Orji, 2002	1	84	Not given

### PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported or page #
TITLE	<u>.</u>		
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	2-3
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	4
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	5
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	5
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	5-7
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	5
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	Appendix 1
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	5-6, Appendix 2
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	6-7
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	5-7
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	7
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	7-8
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g. e <sup>12</sup> ) for each meta analysis com/site/about/guidelines.xhtml	8

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# PRISMA 2009 Checklist

Page	1	of 2	

#	Checklist item	Reported		
		on page #		
15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	7-8		
16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	7-8		
17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	8, Figure 1		
18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	8, Table 1		
19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	8, 9, Figure 2		
20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	9,10 Table 2, Figure 3 Figure S1,S2 Appendix 5, 6		
21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	10, Appendix 3, 4		
22	Present results of any assessment of risk of bias across studies (see Item 15).	8,9 Figure 2		
23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	9,10 Figure S1, S2		
24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	10		
25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias). For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml	11		
-	17   18   19   20   21   21   22   23   23	16       Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.         17       Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.         18       For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.         19       Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).         20       For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.         21       Present results of each meta-analysis done, including confidence intervals and measures of consistency.         22       Present results of any assessment of risk of bias across studies (see Item 15).         23       Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).         24       Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).		

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# PRISMA 2009 Checklist

3						
4 5	Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	12		
6	FUNDING	JNDING				
7 8 9	Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	3		
9 10	From: Moher D, Liberati A, Tetzlaff , doi:10.1371/journal.pmed1000097	J, Altma	an DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med I For more information, visit: www.prisma-statement.org. Page 2 of 2	6(7): e1000097.		
42 43 44 45 46 47			For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml			